Psychosocial consequences of living kidney donation

From screening to intervention

LIEKE WIRKEN

Psychosocial consequences of living kidney donation

From screening to intervention

Lieke Wirken

The work presented in this thesis was carried out within the Radboud Institute for Health Sciences (RIHS), at the Department of Medical Psychology of the Radboud university medical center in Nijmegen, and within the Institute of Psychology, at the Health, Medical and Neuropsychology Unit of Leiden University, the Netherlands.

This PhD research was funded by a grant from the Dutch Kidney Foundation. Thesis printing was sponsored by the 'Nederlandse Transplantatie Vereniging'.

ISBN: 978-94-6361-073-5

Cover design: L. Wirken
Layout and printed by: Optima Grafische Communicatie, Rotterdam, the Netherlands (www.ogc.nl)

Psychosocial consequences of living kidney donation
From screening to intervention

Proefschrift

ter verkrijging van de graad van doctor
aan de Radboud Universiteit Nijmegen
op gezag van de rector magnificus prof. dr. J.H.J.M van Krieken,
volgens besluit van het college van decanen
in het openbaar te verdedigen op woensdag 18 april 2018
om 14.30 uur precies

door

Gerdina (Lieke) Andrea Antonia Wirken
geboren op 13 januari 1985
te Dongen

Promotoren
Prof. dr. A.W.M. Evers (UL)
Prof. dr. L.B. Hilbrands
Prof. dr. A.J. Hoitsma

Copromotor
Dr. H. van Middendorp

Manuscriptcommissie
Prof. dr. W.J.J. Assendelft
Prof. dr. M. Hagedoorn (UMCG)
Dr. F.C.H. d'Ancona

CONTENTS

Chapter 1

General Introduction

The worldwide prevalence of chronic kidney disease has risen to about 13%, partly due to the increase of diabetes and hypertension (1). In end-stage renal disease (ESRD), the patient's kidney function is reduced to less than 10%, and renal replacement therapy is needed for survival. For these patients, two treatment options are available, namely dialysis and transplantation. Kidney transplantation has major advantages for patients in comparison to dialysis treatment, namely a higher life expectancy and better health-related quality of life (HRQoL) (2-4). Also, healthcare costs for patients after transplantation are lower than during dialysis treatment (5). Since the availability of deceased donor kidneys does not meet the demand, there is a waiting list for a deceased donor kidney. Currently, the mean waiting time in the Netherlands is between 2 and 3 years, depending on ABO blood group type (6). A solution for this shortage of deceased donor kidneys is increasing the pool of living donors. Living donor kidney transplantation is currently the best treatment option for most patients with ESRD, as it has higher patient and graft survival rates as compared to deceased donor kidney transplantation (7). Furthermore, the availability of a living donor kidney enables pre-emptive transplantation (i.e., before the start of dialysis treatment), whereas this is seldom possible with a deceased donor kidney. In recent decades, the number of living donor kidney transplantations has increased strongly, with more living than deceased donor kidney transplantations currently being performed in the Netherlands (Figure 1) (8).

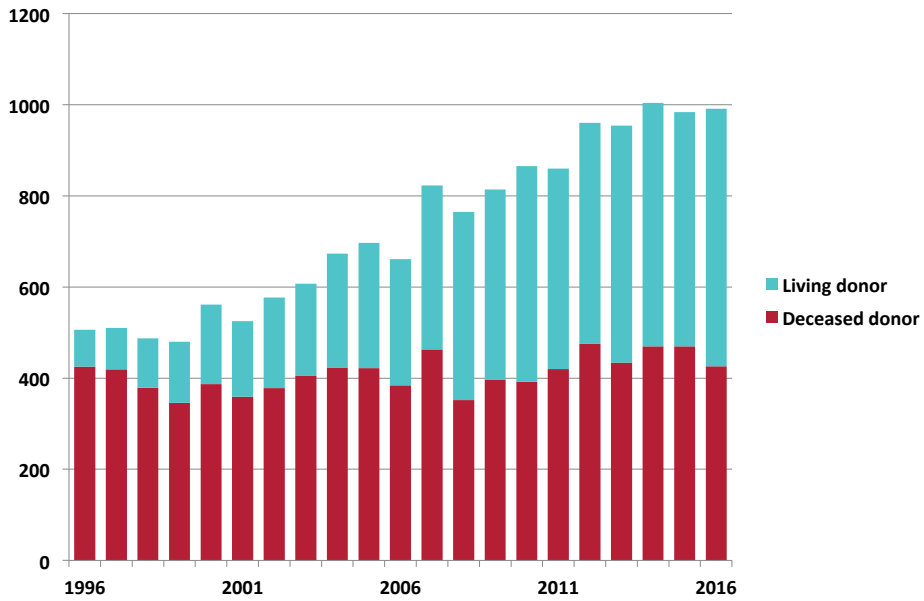


Figure 1. The number of kidney transplantations from both deceased and living donors in the Netherlands
Source: Dutch Transplant Foundation, Annual reports 2000-2016

Donor nephrectomy is an invasive procedure causing temporary physical limitations. Moreover, donating a kidney can have an impact on the psychosocial wellbeing of donors and their relatives. In general, donor candidates are highly motivated to undergo this surgery in order to help the ESRD patient, who is mostly a spouse, child, parent, sibling, or friend, as they have witnessed the influence of the disease on the daily life of the recipient from close-by, and have shared the emotional consequences thereof. There are also anonymous donors who do not know the recipient and who donate altruistically (9-11). Donors can experience the donation as beneficial because of the improved wellbeing of their recipient, which results in a potential improvement of their own HRQoL (12-14), and the enhancement of their self-esteem (14, 15). However, a small group of donors experiences difficulties prior to the surgery or after donation. An early psychosocial screening of donor candidates could minimize these negative consequences of donation. There is currently insufficient data to determine whether there are specific donor risk factors for impaired psychosocial functioning after donation, due mainly to the lack of large and encompassing prospective prediction studies in this population. Consequently, current international guidelines for psychosocial donor evaluation are not standardized. They mostly focus on the assessment of previous or current mental illness, personality characteristics, the ability to give informed consent for donation, decision-making, social-relational factors, and financial issues (16-21). Some guidelines for donor evaluation include certain psychosocial risk factors as absolute contra-indications for donation, while others recommend assessing psychosocial risk factors to identify donors who might benefit from additional support during or after the donation procedure, for example in the case of early graft failure or recipient death (17, 18).

To summarize, living donor kidney transplantation is currently the preferred treatment for most patients with ESRD. Due to the lack of large prospective prediction studies, guidelines for psychosocial donor evaluation are currently not standardized. It is therefore important to identify the most relevant risk factors for impaired longer-term HRQoL after donation, in order to be able to develop psychosocial screening instruments on the basis of these risk factors and to develop tailored interventions for donors who are at risk of psychosocial adjustment problems during or after the donation.

HEALTH-RELATED QUALITY OF LIFE OF LIVING KIDNEY DONORS

Donor candidates are screened for the eligibility to donate, taking both medical and psychosocial aspects into account. Consequently, accepted donors are generally relatively healthy before the donation, mostly healthier than the general population (22-24). Despite a temporary decline in physical health due to the consequences of the surgery,

most donors recover within a few weeks, without persistent physical or psychosocial problems (15, 25). However, a subgroup of donors (5-23%) experiences elevated levels of fatigue or more depressive symptoms after donation, potentially caused by factors such as pre-donation psychological problems (e.g., excessive worrying), donor or recipient complications (26-28), unmet expectations about the donation (14, 29), or problems in the relationship with the recipient or other relatives (17, 30). There is currently insufficient evidence to indicate which factors influence the course of HRQoL during the donation procedure.

Previous studies on the HRQoL of kidney donors have mostly been retrospective, describing a relatively favorable post-donation functioning in the majority of donors (14, 31-36). The prospective studies that have been conducted assessed the course of HRQoL before and after donation using validated questionnaires (15, 37-45). These studies showed somewhat inconsistent results, which may be due to a number of reasons. First, developments in donor nephrectomy techniques, especially the introduction of laparoscopic nephrectomy, have led to smaller wounds and shorter recovery periods, which could have influenced the donor's physical and potentially also psychosocial recovery after surgery (43, 46-48). Second, there has been a shift in acceptance criteria of donors, resulting in a higher proportion of donors with a higher age, body mass index, or blood pressure (49), which may impact on physical and psychosocial long-term outcomes of donors (50, 51). Third, the increasing number of genetically unrelated and anonymous donors will be associated with specific types or the absence of donor-recipient relationships, which might influence differences in donor HRQoL described in prospective studies (10, 35, 52). Therefore, this thesis describes in a systematic review and meta-analysis a systematic evaluation of the course of HRQoL before and after kidney donation as reported in previous studies (Chapter 2).

From a methodological point of view, the course of HRQoL before and after donation has mainly been assessed using generic quality of life instruments (e.g., Short Form Health Survey-36 or World Health Organization Quality of Life Questionnaire) that are not specifically focused on the donor's situation (38, 41, 43). However, specific donation-related outcomes that are not captured by generic measures could be of significant value in the clinical care for living kidney donors (e.g., recipient-related functioning or feelings of regret after donation) (29). Consequently, in the current thesis, the HRQoL course from before to after donation was examined in a large prospective study conducted in seven Dutch transplantation centers, using a comprehensive set of both generic and donation-specific measurements (Chapter 3).

PRE-DONATION COGNITIONS OF DONOR CANDIDATES

Before donor candidates are registered at the transplantation center for a possible donation, a process of decision-making has taken place in which the perceived risks and benefits of a potential donation are weighed. During this decision-making process, cognitions about the motivation for donation, the expectations of the donation and transplantation, and potential worries are explored. The motivation for donation is generally based on a desire to improve the wellbeing of a relative suffering from ESRD. Other donor motives could include personal beliefs or religious convictions, an increase in the donor's self-esteem, or an improvement of the donor's own wellbeing by decreasing the disease burden of the intended recipient (12, 13, 53). Also, motivations for donation could be influenced by feelings of moral duty or perceived external pressure, e.g., when someone is the only suitable donor within the family of the recipient (12, 54). Besides donor motives, donor expectations could determine the decision to donate. Most donors expect to improve the recipient's health, but some donors also expect personal benefits or advantages in social relationships as a consequence of the donation (55). In the majority of cases, the expectations relating to donation are realistic and, retrospectively, donors perceived the donation procedure to be in line with their expectations (15). When the expectations of donors are not met, this can be related to disappointment about recipient outcomes (29). Concerning potential worries about the donation, previous studies reported concerns about the physical functioning of the recipient after transplantation, about the function of the donor's remaining kidney, about the results of the medical evaluation as part of the donor eligibility screening (54), and about physical consequences of donation (14).

Such pre-donation cognitions could potentially influence the course of HRQoL during or after the donation procedure. To date, pre-donation cognitions have mainly been assessed using qualitative methods, because quantitative instruments that examine donor motivations, expectations, and donation-related worries were limited to those focusing on specific aspects of these cognitions (55). A valid instrument that assesses various pre-donation cognitions of donor candidates could be used to improve the psychosocial donor evaluation, for example to make potential donors aware of their own thoughts and feelings regarding the upcoming donation. A questionnaire measuring the donor's motivation for donation, the expectations of donation, and potential worries about the donation was therefore developed as part of this thesis; this questionnaire was subsequently validated in a large sample of potential living kidney donors (Chapter 4). In addition, the predictive value of these pre-donation cognitions on impaired longer-term HRQoL after donation was examined for the first time as part of an encompassing set of predictors in the large prospective study (Chapter 5).

PREDICTORS OF LONGER-TERM ADJUSTMENT PROBLEMS

Traditionally, the eligibility screening of potential living kidney donors has mainly been medically oriented, focusing on physical characteristics to judge whether potential donors are suitable for donation. Psychosocial evaluation was often conducted only when indications were found during the medical screening. Nowadays, there is consensus that besides this medical donor evaluation, a psychosocial donor evaluation should also be conducted as part of the standard screening procedure, due to the impact of donation on the donor's physical and psychological functioning and relationships with others (56-58). However, prospective studies that systematically investigate potential predictors of impaired longer-term functioning after donation are scarce (59, 60), as indicated in the systematic review in Chapter 2. As a result, current guidelines on psychosocial donor evaluation are mostly not evidence-based, which leads to inconsistencies in the content and assessment methods of psychosocial evaluation among transplantation centers. More comprehensive prospective prediction studies are needed to identify the most relevant donor characteristics predictive of impaired longer-term functioning after donation.

Due to the scarcity of scientific evidence about potential risk factors for longer-term adjustment problems in living kidney donors, current psychosocial screening is mainly based on the clinical judgment of transplant professionals. However, the accuracy of these mostly intuitive and implicit risk judgments is unknown. Furthermore, it is unknown how the predictive value for longer-term HRQoL after donation of these clinical risk judgments compares with that of screening questionnaires and whether the addition of brief standardized screening questionnaires could improve the prediction of longer-term HRQoL after donation to a relevant degree. Therefore, the (additive) predictive value of clinical risk judgments and donor self-report questionnaires up to 12 months after donation was examined in a large sample of living kidney donors (Chapter 5).

INTERVENTIONS FOR DONORS WITH A RISK PROFILE

A number of studies on the psychosocial wellbeing of donors emphasize the importance of psychosocial care for specific donors or potential donors with elevated distress levels (26, 61, 62). However, there are currently hardly no interventions available for (potential) donors (63), and those available are mostly focused on stimulating donor recruitment (64, 65).

Based on the types of problems that are reported by some donors, such as fatigue, depressed mood, and social-relational difficulties, psychosocial interventions for this

group should focus on strategies to deal with the impact of the donation on daily life. Cognitive-behavioral therapy (CBT) is an evidence-based psychological treatment paradigm, which is used to treat mental health conditions, focusing on the replacement of maladaptive cognitions and coping strategies into more adaptive cognitions and behaviors (66-68). Previous research found that cognitive-behavioral therapy provided via the internet (Internet-based Cognitive-Behavioral Therapy or ICBT) could be as effective as face-to-face treatments in improving physical and psychological functioning in patients with mental and physical health problems (69-71). When these ICBT interventions for patients with somatic conditions are slightly adjusted and include donation-related themes, they could also be useful for potential donors and donors with adjustment problems. The acceptability and effectiveness of (I)CBT can be possibly further increased by tailoring the interventions to the specific risk and resilience factors of individuals as well as by therapist guidance (72, 73). There is currently no encompassing cognitive-behavioral intervention available for donors and potential donors with a high-risk profile for longer-term adjustment problems. As part of this thesis, a guided and tailored ICBT intervention, directed at treating donation-related adjustment problems, is developed and evaluated in a small group of donors (Chapter 6).

AIM AND OUTLINE OF THE THESIS

The main purpose of the research performed in this thesis was to identify and guide potential donors at risk of experiencing adjustment problems on the longer-term after donation. Therefore, the main objectives of the studies presented in this thesis were to develop and validate a psychosocial screening instrument and tailored intervention to identify and treat donors at risk of longer-term adjustment problems.

Chapter 2 includes a review and meta-analysis summarizing the existing literature on longer-term HRQoL of living kidney donors. In this chapter, the current state of the knowledge on the course of HRQoL of donors and potential risk factors for poorer longer-term functioning after donation was deduced from previous literature. **Chapter 3** presents the results of a prospective multicenter study on the course of HRQoL of living kidney donors before donation and 6 and 12 months after donation using both generic quality of life instruments as well as donation-specific questionnaires. Donor- and recipient-related donation consequences from the donor's perspective, and regret about the donation decision are also examined. **Chapter 4** describes the development of a new questionnaire on pre-donation cognitions (the motivation for donation, the expectations of donation, and worries about donation). This chapter also reports the validation of the newly developed questionnaire in a large group of potential kidney donors from seven Dutch transplantation centers. **Chapter 5** presents the relative

contribution of clinical risk judgments by transplant professionals, a comprehensive account of pre-, intra-, and post-donation characteristics of the donor, and the donor's self-report measures to the prediction of impaired longer-term HRQoL of living kidney donors. **Chapter 6** describes the transition from donor assessment to donor intervention, and comprises the development and feasibility testing of an eHealth intervention for donors and potential donors with a high-risk profile. Concluding this thesis, **Chapter 7** summarizes the main findings of the studies described, and **Chapter 8** provides a general discussion of these findings, as well as a critical reflection on the theoretical and clinical implications, and directions for future research.

REFERENCES

1. Hill NR, Fatoba ST, Oke JL, et al. Global prevalence of chronic kidney disease - a systematic review and meta-analysis. PLoS One. 2016; 11: e0158765.
2. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med. 1999; 341: 1725-1730.
3. Evans RW, Manninen DL, Garrison LP, Jr., et al. The quality of life of patients with end-stage renal disease. N Engl J Med. 1985; 312: 553-559.
4. Landreneau K, Lee K, Landreneau MD. Quality of life in patients undergoing hemodialysis and renal transplantation--a meta-analytic review. Nephrol Nurs J. 2010; 37: 37-44.
5. Laupacis A, Keown P, Pus N, et al. A study of the quality of life and cost-utility of renal transplantation. Kidney Int. 1996; 50: 235-242.
6. The Dutch Transplant Foundation. 2017.
7. Hariharan S, Johnson CP, Bresnahan BA, Taranto SE, McIntosh MJ, Stablein D. Improved graft survival after renal transplantation in the United States, 1988 to 1996. N Engl J Med. 2000; 342: 605-612.
8. Annual Report Dutch Transplant Foundation.2016.
9. Nelson EW, Mone MC, Nelson ET, Hansen HJ, Gawlick U, Alder S. Evolution of trends in the live kidney transplant donor-recipient relationship. Transplant Proc.2013; 45: 57-64.
10. Rodrigue JR, Schutzer ME, Paek M, Morrissey P. Altruistic kidney donation to a stranger: psychosocial and functional outcomes at two US transplant centers. Transplantation. 2011; 91: 772-778.
11. Sharif A. Unspecified kidney donation--a review of principles, practice and potential. Transplantation. 2013; 95: 1425-1430.
12. Lennerling A, Forsberg A, Nyberg G. Becoming a living kidney donor. Transplantation. 2003; 76: 1243-1247.
13. Agerskov H, Bistrup C, Ludvigsen MS, Pedersen BD. Living kidney donation: considerations and decision-making. J Ren Care. 2014; 40: 88-95.
14. Andersen MH, Bruserud F, Mathisen L, Wahl AK, Hanestad BR, Fosse E. Follow-up interviews of 12 living kidney donors one yr after open donor nephrectomy. Clin Transplant. 2007; 21: 702-709.
15. Garcia MF, Andrade LG, Carvalho MF. Living kidney donors--a prospective study of quality of life before and after kidney donation. Clin Transplant. 2013; 27: 9-14.
16. Clinical guidelines for living donor kidney transplantation. Health Canada. 2016.
17. Joint Working Party of The Brithish Transplantation Society and The Renal Association. United Kingdom Guidelines for living donor kidney transplantation. 2011.
18. Kanellis J. The CARI guidelines. Justification for living donor kidney transplantation. Nephrology. 2010; 15 Suppl 1: S72-79.
19. The Canadian Council for Donation and Transplantation. Enhancing living donation: a Canadian forum. Vancouver, British Columbia.2006.
20. Organ Procurement and Transplantation Network (OPTN) Policies. 2017.
21. Duerinckx N, Timmerman L, Van Gogh J, et al. Predonation psychosocial evaluation of living kidney and liver donor candidates: a systematic literature review. Transpl Int. 2014; 27: 2-18.
22. Klop KW, Dols LF, Weimar W, Dooper IM, JN IJ, Kok NF. Quality of life of elderly live kidney donors. Transplantation. 2013; 96: 644-648.

23. Kroencke S, Fischer L, Nashan B, Herich L, Schulz KH. A prospective study on living related kidney donors' quality of life in the first year: choosing appropriate reference data. Clin Transplant. 2012; 26: E418-427.
24. Gross CR, Messersmith EE, Hong BA, et al. Health-related quality of life in kidney donors from the last five decades: results from the RELIVE study. Am J Transplant. 2013; 13: 2924-2934.
25. Wirken L, van Middendorp H, Hooghof CW, et al. The Course and Predictors of Health-Related Quality of Life in Living Kidney Donors: A Systematic Review and Meta-Analysis. Am J Transplant. 2015; 15: 3041-3054.
26. Giessing M, Reuter S, Schonberger B, et al. Quality of life of living kidney donors in Germany: a survey with the Validated Short Form-36 and Giessen Subjective Complaints List-24 questionnaires. Transplantation. 2004; 78: 864-872.
27. Timmerman L, Laging M, Timman R, et al. The impact of the donors' and recipients' medical complications on living kidney donors' mental health. Transpl Int. 2016; 29: 589-602.
28. Jacobs C, Johnson E, Anderson K, Gillingham K, Matas A. Kidney transplants from living donors: how donation affects family dynamics. Adv Ren Replace Ther. 1998; 5: 89-97.
29. Rodrigue JR, Paek M, Whiting J, et al. Trajectories of perceived benefits in living kidney donors: association with donor characteristics and recipient outcomes. Transplantation. 2014; 97: 762-768.
30. Reimer J, Rensing A, Haasen C, Philipp T, Pietruck F, Franke GH. The impact of living-related kidney transplantation on the donor's life. Transplantation. 2006; 81: 1268-1273.
31. Clemens K, Boudville N, Dew MA, et al. The long-term quality of life of living kidney donors: a multicenter cohort study. Am J Transplant. 2011; 11: 463-469.
32. Fournier C, Pallet N, Cherqaoui Z, et al. Very long-term follow-up of living kidney donors. Transpl Int. 2012; 25: 385-390.
33. de Groot IB, Stiggelbout AM, van der Boog PJ, Baranski AG, Marang-van de Mheen PJ, group PA-s. Reduced quality of life in living kidney donors: association with fatigue, societal participation and pre-donation variables. Transpl Int. 2012; 25: 967-975.
34. Albertsmeyer S, Renner FC, Yildiz S, et al. One hundred six live kidney donors in a single German transplantation center: renal, physical, and psychological follow-up. Transplant Proc. 2010; 42: 3992-3993.
35. Jowsey SG, Jacobs C, Gross CR, et al. Emotional well-being of living kidney donors: findings from the RELIVE Study. Am J Transplant.2014; 14: 2535-2544.
36. Feltrin A, Pegoraro R, Rago C, et al. Experience of donation and quality of life in living kidney and liver donors. Transpl Int. 2008; 21: 466-472.
37. Aguiar WF, Passerotti CC, Claro JF, et al. Mini-incisions by lombotomy or subcostal access in living kidney donors: a randomized trial comparing pain, safety, and quality of life. Clin Transplant. 2007; 21: 269-276.
38. Andersen MH, Mathisen L, Veenstra M, et al. Quality of life after randomization to laparoscopic versus open living donor nephrectomy: long-term follow-up. Transplantation. 2007; 84: 64-69.
39. Bahler CD, Sundaram CP. Quality of life following laparoscopic living-donor nephrectomy. JSLS. 2013; 17: 273-278.
40. Bargman V, Sundaram CP, Bernie J, Goggins W. Randomized trial of laparoscopic donor nephrectomy with and without hand assistance. J Endourol. 2006; 20: 717-722.
41. Bergman S, Feldman LS, Mayo NE, et al. Measuring surgical recovery: the study of laparoscopic live donor nephrectomy. Am J Transplant. 2005; 5: 2489-2495.
42. Chien CH, Wang HH, Chiang YJ, Chu SH, Liu HE, Liu KL. Quality of life after laparoscopic donor nephrectomy. Transplant Proc. 2010; 42: 696-698.

43. Dols LF, Ijzermans JN, Wentink N, et al. Long-term follow-up of a randomized trial comparing laparoscopic and mini-incision open live donor nephrectomy. Am J Transplant. 2010; 10: 2481-2487.
44. Dols LF, Kok NF, d'Ancona FC, et al. Randomized controlled trial comparing hand-assisted retroperitoneoscopic versus standard laparoscopic donor nephrectomy. Transplantation. 2014; 97: 161-167.
45. Frade IC, Fonseca I, Dias L, et al. Impact assessment in living kidney donation: psychosocial aspects in the donor. Transplant Proc. 2008; 40: 677-681.
46. Klop KW, Kok NF, Dols LF, et al. Can right-sided hand-assisted retroperitoneoscopic donor nephrectomy be advocated above standard laparoscopic donor nephrectomy: a randomized pilot study. Transpl Int. 2014; 27: 162-169.
47. Kok NF, Alwayn IP, Tran KT, Hop WC, Weimar W, Ijzermans JN. Psychosocial and physical impairment after mini-incision open and laparoscopic donor nephrectomy: A prospective study. Transplantation. 2006; 82: 1291-1297.
48. Nicholson ML, Elwell R, Kaushik M, Bagul A, Hosgood SA. Health-related quality of life after living donor nephrectomy: a randomized controlled trial of laparoscopic versus open nephrectomy. Transplantation. 2011; 91: 457-461.
49. Mandelbrot DA, Pavlakis M, Danovitch GM, et al. The medical evaluation of living kidney donors: a survey of US transplant centers. Am J Transplant. 2007; 7: 2333-2343.
50. Minnee RC, Bemelman WA, Polle SW, et al. Older living kidney donors: surgical outcome and quality of life. Transplantation. 2008; 86: 251-256.
51. Reese PP, Feldman HI, McBride MA, Anderson K, Asch DA, Bloom RD. Substantial variation in the acceptance of medically complex live kidney donors across US renal transplant centers. Am J Transplant. 2008; 8: 2062-2070.
52. Baskin JH. Giving until it hurts?: Altruistic donation of solid organs. J Am Acad Psychiatry Law. 2009; 37: 377-379.
53. Boulware LE, Ratner LE, Troll MU, et al. Attitudes, psychology, and risk taking of potential live kidney donors: strangers, relatives, and the general public. Am J Transplant. 2005; 5: 1671-1680.
54. Lennerling A, Forsberg A, Meyer K, Nyberg G. Motives for becoming a living kidney donor. Nephrol Dial Transplant. 2004; 19: 1600-1605.
55. Rodrigue JR, Guenther R, Kaplan B, Mandelbrot DA, Pavlakis M, Howard RJ. Measuring the expectations of kidney donors: initial psychometric properties of the Living Donation Expectancies Questionnaire. Transplantation. 2008; 85: 1230-1234.
56. Dew MA, Jacobs CL, Jowsey SG, et al. Guidelines for the psychosocial evaluation of living unrelated kidney donors in the United States. Am J Transplant. 2007; 7: 1047-1054.
57. Andrews PA, Burnapp L, Manas D, et al. Summary of the British Transplantation Society/Renal Association U.K. guidelines for living donor kidney transplantation. Transplantation. 2012; 93: 666-673.
58. Ismail SY, Duerinckx N, van der Knoop MM, et al. Toward a Conceptualization of the Content of Psychosocial Screening in Living Organ Donors: An Ethical Legal Psychological Aspects of Transplantation Consensus. Transplantation. 2015; 99: 2413-2421.
59. Smith GC, Trauer T, Kerr PG, Chadban SJ. Prospective psychosocial monitoring of living kidney donors using the Short Form-36 health survey: results at 12 months. Transplantation. 2004; 78: 1384-1389.
60. Timmerman L, Timman R, Laging M, et al. Predicting mental health after living kidney donation: The importance of psychological factors. Br J Health Psychol: 2016; 21: 533-554.

61. van Hardeveld E, Tong A, Cari. The CARI guidelines. Psychosocial care of living kidney donors. Nephrology. 2010; 15 Suppl 1: S80-87.
62. Smith GC, Trauer T, Kerr PG, Chadban SJ. Prospective psychosocial monitoring of living kidney donors using the SF-36 health survey. Transplantation. 2003; 76: 807-809.
63. Dew MA, DiMartini AF, DeVito Dabbs AJ, et al. Preventive intervention for living donor psychosocial outcomes: feasibility and efficacy in a randomized controlled trial. Am J Transplant. 2013; 13: 2672-2684.
64. Rodrigue JR, Pavlakis M, Egbuna O, Paek M, Waterman AD, Mandelbrot DA. The "House Calls" trial: a randomized controlled trial to reduce racial disparities in live donor kidney transplantation: rationale and design. Contemp Clin Trials. 2012; 33: 811-818.
65. Alvaro EM, Siegel JT, Crano WD, Dominick A. A mass mediated intervention on Hispanic live kidney donation. J Health Commun. 2010; 15: 374-387.
66. Butler AC, Chapman JE, Forman EM, Beck AT. The empirical status of cognitive-behavioral therapy: a review of meta-analyses. Clin Psychol Rev. 2006; 26: 17-31.
67. Reinecke MA, Ryan NE, DuBois DL. Cognitive-behavioral therapy of depression and depressive symptoms during adolescence: a review and meta-analysis. J Am Acad Child Adolesc Psychiatry. 1998; 37: 26-34.
68. Tatrow K, Montgomery GH. Cognitive behavioral therapy techniques for distress and pain in breast cancer patients: a meta-analysis. J Behav Med. 2006; 29: 17-27.
69. Cuijpers P, van Straten A, Andersson G. Internet-administered cognitive behavior therapy for health problems: a systematic review. J Behav Med. 2008; 31: 169-177.
70. Postel MG, de Haan HA, De Jong CA. E-therapy for mental health problems: a systematic review. Telemed J E Health. 2008; 14: 707-714.
71. Spek V, Cuijpers P, Nyklicek I, Riper H, Keyzer J, Pop V. Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. Psychol Med. 2007; 37: 319-328.
72. Johansson R, Sjoberg E, Sjogren M, et al. Tailored vs. standardized internet-based cognitive behavior therapy for depression and comorbid symptoms: a randomized controlled trial. PLoS One. 2012; 7: e36905.
73. Turk DC. Customizing treatment for chronic pain patients: who, what, and why. Clin J Pain. 1990; 6: 255-270.

Chapter 2

The course and predictors of health-related quality of life in living kidney donors: a systematic review and meta-analysis

Wirken L, van Middendorp H, Hooghof CW, Rovers MM, Hoitsma AJ, Hilbrands LB, Evers AWM

The American Journal of Transplantation 2015; 15: 3041-54.

ABSTRACT

A better understanding of the course and risk factors for impaired long-term health-related quality of life (HRQoL; i.e., physical, psychological, and social-relational functioning) after kidney donation might help clinicians improve the care of live kidney donors. This systematic review and meta-analysis summarizes prospective studies about the course and predictors of HRQoL in living kidney donors. Studies indicate that shortly after donation, donors have lower HRQoL, with minor to moderate changes in psychological and social-relational functioning and major changes in physical functioning. At 3-12 months after donation, HRQoL returned to baseline or was slightly reduced, particularly for fatigue, but scores were still comparable to general population norms. Results were mainly robust across surgery techniques. A limited number of studies examined risk factors for impaired HRQoL, with low psychological functioning before donation as the most consistent predictor. Based on these results, clinicians can inform potential donors that, on average, kidney donors have high long-term HRQoL; however, donors with low psychological functioning at baseline are those most at risk of impaired long-term HRQoL. Future studies should focus on other potentially relevant predictors of post-donation HRQoL, including donor eligibility criteria and donor-recipient relationships, to optimize screening and interventions for donors at risk.

INTRODUCTION

The high percentages of living donor kidney transplantations worldwide have prompted research into kidney donors' health-related quality of life (HRQoL), consisting of physical, psychological and social-relational functioning (1). Donors have been found to have high HRQoL before donation (2-4), often better than that of the general population, probably because of the stringent medical screening for kidney donor eligibility. After donation, however, approximately 5%-25% of donors experience problems with physical or psychosocial functioning, such as depressed mood, fatigue or pain (5-7). A previous systematic review of mostly cross-sectional and a few prospective studies concluded that most donors experienced no change or improvement in psychosocial functioning on average at 4 years after donation but that a small group of donors reported adverse psychosocial outcomes (5).

After this previous review, new prospective studies and randomized controlled trials were published addressing the HRQoL of living kidney donors (8-14). Moreover, advances in surgery techniques, such as minimally invasive techniques, and expansion of donor eligibility criteria (e.g., acceptance of donors at higher ages, body mass index (BMI), or blood pressure), may have affected HRQoL (15-17). In addition, because impaired HRQoL after donation has been found, it is relevant to know potential predictors to guide screening and interventions for donors at risk to prevent impaired functioning after donation. Currently, guidelines to select eligible living kidney donors are based mainly on physical and not on psychosocial criteria (2, 15 ,18-22). Consequently, we conducted an updated systematic review and meta-analysis of the current literature 1) on the course of HRQoL of living kidney donors from before to after donation and 2) on predictors of post-donation HRQoL.

METHODS

Literature search strategy and inclusion criteria

PubMed, Embase, Cinahl, and PsycINFO databases from 1990 until February 2014 were systematically searched, using *living kidney donors*, *psychological factors*, and *quality of life* as keywords. In addition, the reference lists of included studies and review articles were examined for other potentially relevant articles. All prospective studies published in English peer-reviewed journals investigating HRQoL before and after donation and using validated self-report questionnaires were included. Details of the protocol for this systematic review and meta-analysis were registered on PROSPERO (http://www.crd.york.ac.uk/ PROSPERO/display_record.asp?ID=CRD42013006517).

HRQoL domains

The questionnaires used to assess different HRQoL domains are reported in Table 1. Physical functioning was assessed as *physical disability*, defined as physical limitations in daily activities due to health; *pain*, defined as the frequency and interference of pain and discomfort in performing daily activities; and *fatigue*, defined as a lack of energy and different fatigue dimensions (physical and mental fatigue, reduced activities and motivation). *Psychological functioning* included feelings of anxiety, nervousness or depression. *Social-relational functioning* concerned limitations of social activities due to health.

Table 1. Questionnaires and timing of pre-donation and post-donation HRQoL assessments of the studies assessing the course of HRQoL

Author (year)	HRQoL Questionnaires	Timing pre-donation HRQoL assessment (time to donation)	Timing post-donation HRQoL assessment(s) (time after donation)
Aguiar et al. (2007)	SF36	NA	1 and 3 months
Andersen et al. (2007)	SF36	1-2 day(s)	1 and 12 months
Bahler et al. (2013)	SF36	NA	1, 4, and 7 months
Bergman et al. (2005)	SF36	NA	4 weeks (*M*= 29 days)
Chien et al. (2010)	SF36	92.9 ± 5.0 days	3 months (80.4 ± 16.6 days)
Dols et al. (2010)	SF36 MFI-20	NA	6 years (range 1-8)
Dols et al. (2014)	SF36	NA	1, 3*, 6*, and 12 months
Frade et al. (2008)	SF36 SAS SDS	NA	18.8 ± 12.8 months
Garcia et al. (2013)	SF36	20 ± 27 days	3 months (126 ± 89 days) and 12 months (445 ± 164 days)
Guleria et al. (2011)	WHOQOL Bref HADS	2 weeks	6 months
Klop et al. (2013-I)	SF36	NA	1, 3, 6, and 12 months*
Klop et al. (2013-II)	SF36	1 day	1 and 12 months
Kok et al. (2006-I)	SF36 MFI-20	1 day	1, 3, 6, and 12 months
Kok et al. (2006-II)	SF36 MFI-20 EQ-5D	1 day	1, 3, 6, and 12 months*
Kroencke et al. (2012)	SF36 HADS	126 ± 112 days	3 months (96 ± 22 days) and 12 months (381 ± 31 days)
Kurien et al. (2011)	SF36	1 month	6 months
Lopes et al. (2011)	SAS SDS	NA	≥ 12 months*
Lopes et al. (2013)	SF36	NA	≥ 12 months

Table 1. Questionnaires and timing of pre-donation and post-donation HRQoL assessments of the studies assessing the course of HRQoL (continued)

Author (year)	HRQoL Questionnaires	Timing pre-donation HRQoL assessment (time to donation)	Timing post-donation HRQoL assessment(s) (time after donation)
Lumsdaine et al. (2005)	WHOQOL	NA	6 weeks and 12 months
Massey et al. (2010)	SCL-90	NA	2.3 years (3-97 months)
Minnee et al. (2008)	SF36 MFI-20 VAS Pain	NA	SF36: 1, 3, 6, and 12 months MFI-20: 1, 3, 6, and 12 months VAS pain: 28 days
Minz et al. (2005)	BDI STAI SSQ	NA	3 months
Nicholson et al. (2011)	SF36	1 day	6 weeks
Smith et al. (2003)	SF36	NA	4 months
Smith et al. (2004)	SF36	NA	4 and 12 months
Timmerman et al. (2013)	SCL-90	9 months (range 2-13)	19 months (range 3-36)
Vemuru Reddy et al. (2011)	WHOQOL	2 weeks	6 months
Virzi et al. (2007)	SF36	1 month	4 months
Walton-Moss et al. (2007)	SF36	NA	6 and 12 months*

Note. NA: data not available, *: data not available for meta-analysis
BDI, Beck Depression Inventory (Beck, 1961); EQ-5D, EuroQol 5D (The Euroqol group, 1990); HADS, Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983); MFI-20, Multidimensional Fatigue Inventory (Smets, 1995); SAS, Zung Self-rating Anxiety Scale (Zung, 1971); SCL-90, Symptom Checklist-90 (Derogatis, 1973); SDS, Zung Self-rating Depression Scale (Zung, 1965); SF36, Short Form-36 Health Survey (Ware & Sherbourne, 1992); SSQ, Social Support Questionnaire (Sarason, 1983); STAI, State-Trait Anxiety Inventory (Spielberger, 1983); VAS, visual analogue scale (Freyd, 1923); WHOQoL-Bref, World Health Organization quality of life brief questionnaire (The WHOQOL Group, 1994).

Data extraction and study quality assessment

The following data were extracted from the included studies: data collection period and country, number of living donors, demographic variables, donor-recipient relationship, surgery techniques, questionnaires, assessment points and HRQoL outcome measures. Short Form-36 Health Survey (SF-36) physical and mental component summary scores were categorized as physical disability and psychological functioning, respectively (11, 23). When surgery techniques were not mentioned, study authors were contacted.

For the course analyses, post-donation assessments were classified into three periods: the early postoperative period (months 1-2), short-term functioning (months 3-6), and long-term functioning (≥12 months).

Two authors (LW and HvM) independently assessed the risk of bias of included studies using the Cochrane risk of bias criteria (24). Potential differences were discussed until

consensus was reached. Two domains were scored: 1) attrition bias, based on incomplete outcome data (low risk: donors with and without missing data were compared on outcomes; high risk: no reasons for dropout mentioned or data missing potentially related to outcomes; unclear risk: insufficient information) and 2) other potential sources of bias, namely, range of post-donation assessment period (low risk: standardized timing; high risk: very broad standard deviation of timing; unclear risk: broad variation of timing but within one period) and the use of validated questionnaires (low risk: validated questionnaires; high risk: no validated questionnaires; unclear risk: potentially biased assessment). Initially, studies with either a high or low risk of bias (study quality) were all included to assess the course of HRQoL. Subsequently, sensitivity analyses were used to explore the robustness of the main findings using high- and low-quality studies separately.

Data synthesis and analyses

The generic inverse variance analysis methodology for meta-analysis of within-subject designs was applied to analyze HRQoL changes from pre-donation to the three post-donation assessment periods, using standardized mean differences (SMDs or Hedges' g) and standard errors or standard deviations of the SMDs to calculate effect sizes (ESs). An ES of 0.2 represented a small effect, 0.5 represented a medium effect, and 0.8 represented a large effect (25). If data to calculate ESs were not reported, study authors were contacted; some studies had to be excluded because of authors' non-response (18,26) or data not being provided (4,27). Because of repeated assessments within donors, an average correlation of r=0.5 was imputed between pre- and post-donation HRQoL. Because correlations were generally not reported, correlation coefficients of 0.1 and 0.9 were also examined to explore the robustness of the effects. All HRQoL scores were scaled in the direction of negative SMDs representing a decline of HRQoL over time. In case of between-study heterogeneity (I^2) <70%, fixed-effects models were used; otherwise, random-effects models were used (28).

Analyses were conducted using Review Manager version 5.3 (29). To frame the results, the clinical significance of the pre- to post-donation assessment changes was examined by comparing change scores with clinical relevance norms of the psychometric instruments applied in the included studies. The SF-36, for example, was the most used instrument to assess HRQoL, with manuals reporting a 5-point difference as clinically relevant (30-34).

To explore the impact of surgery techniques on HRQoL course, they were categorized as *laparoscopic donor nephrectomy* (LDN; standard laparoscopic and hand-assisted laparoscopic donor nephrectomy [HALN]), *mini-incision donor nephrectomy* (MIDN; incisions <15 cm), and *open donor nephrectomy* (ODN; with or without rib resection). When data were reported on two surgery techniques within one category (e.g., HALN and LDN), the data of the overall most frequently used technique was included for meta-analysis,

after which it was explored whether results changed when the other technique was included. If multiple questionnaires within one HRQoL domain were assessed, the overall most frequently used questionnaire across all studies was initially included in the meta-analysis. Subsequently, sensitivity analyses were conducted to test the robustness of the main findings when using the other questionnaires.

RESULTS

Literature search

Our search yielded 2845 publications, of which 57 full-text articles were reviewed for eligibility; 23 were excluded (Figure 1). The 34 remaining studies had at least one assessment before and after donation: 25 (74%) on HRQoL course, five (15%) on predictors, and four (12%) on course and predictors.

Table 2 describes characteristics of the 34 included studies, which were published between 2002 and 2014. In total, 3201 living kidney donors participated in the included studies, with sample sizes varying from 14 to 501 (median sample size: n=97). Two studies assessed the same cohort of donors (18,46). Donors had a median age of 47.4 years (range 18-94 years), and an average of 60% of donors were female (range 43%-100%). The largest percentage of studies was conducted in the Netherlands (29%), followed by the United States (15%) and India (12%). Response rates at the first assessment varied between 37% and 100%, and dropout rates at the follow-up assessment varied between 0% and 81%.

Study quality assessment

The response rates of the included studies were generally high, with a mean response rate across all studies of 89%. The mean of percentage of dropouts on the last assessment point was 20%. The attrition bias was low in 47% of studies, unclear in 38% of studies, and high in 15% of studies. Other sources of bias (i.e., range of post-donation assessment period and the use of validated questionnaires) were low in 70% of studies, unclear in 9% of studies, and high in 21% of studies (Figures S1 and S2).

Study results

Course of HRQoL: The timing of pre-donation HRQoL assessments was not specified in 16 studies (55%) and varied between 1 day and 9 months before donation in the other studies. The timing of post-donation assessments varied between 1 month and 6 years after donation (Table 1).

Table 3 summarizes the meta-analytical findings on the course of the physical, psychological and social-relational HRQoL domains.

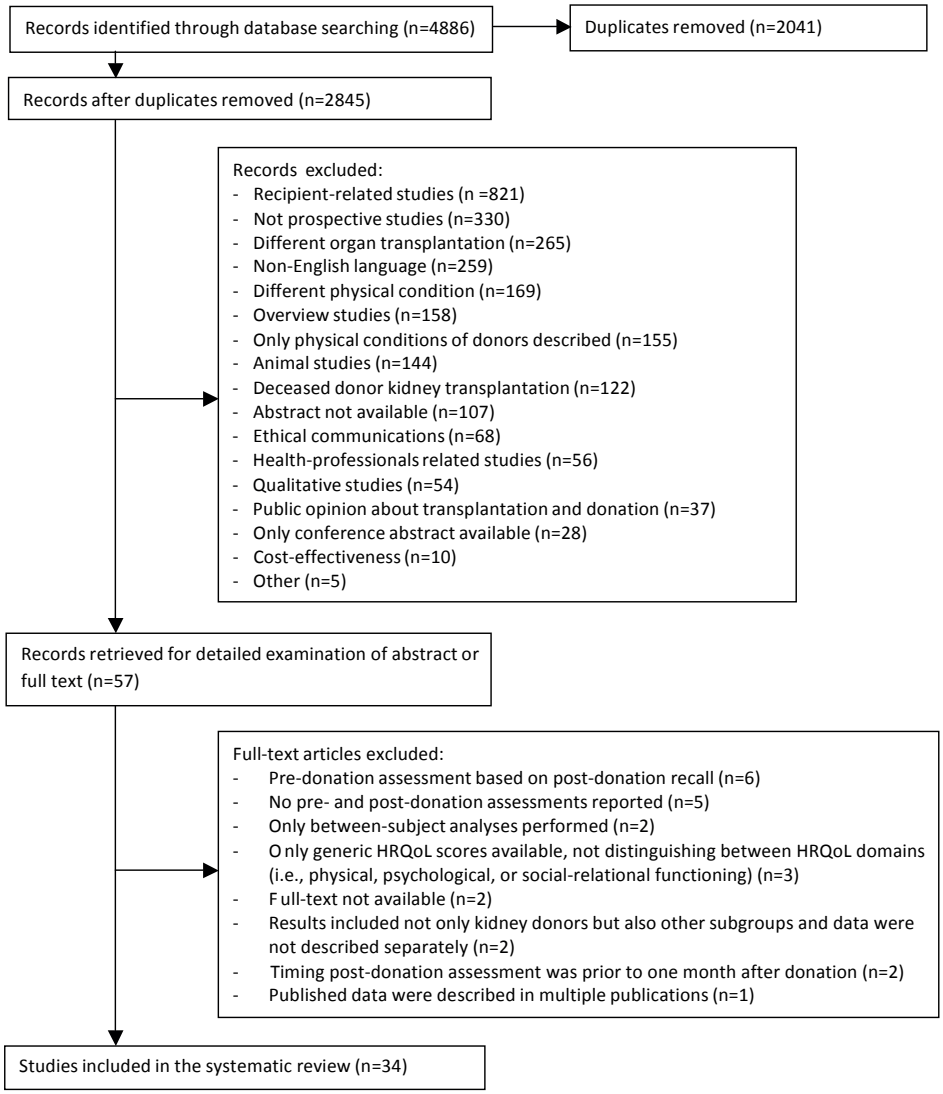


Figure 1. Flow Chart

Table 2. Characteristics of studies included in the systematic review and meta-analysis for both course and prediction of health-related quality of life

Author (year)	Study Purpose	Course data available for meta-analysis	Country	N	Year data collection	Percent female, %	Donor age (range)	Surgery Technique	Donor type	Multi-center	Response rate	Drop-out last assessment
Aguiar et al. (2007)	1	Yes	Brazil	60	2003	68%	41.6 ± 8.9	MIDN: 100%	Related: 92% Unrelated: 8%	No	NA	10%
Andersen et al. (2007)	1	Yes	Norway	122	2001-2004	55%	45.5	ODN: 48% LDN: 52%	Related: 80% Unrelated: 20%	No	51%	21%
Bahler et al. (2013)	1+2	Yes	USA	101	2006-2010	56%	38 (19-62)	LDN: 100%	Related: 76% Unrelated: 24%	No	NA	76%
Bergman et al. (2005)	1	Yes	Canada	35	2001-2004	57%	40 (31-49)	LDN: 100%	NA	No	97%	8%
Chien et al. (2010)	1+2	Yes	Taiwan	14	2005-2008	50%	45.3 (28-62)	LDN: 100%	Related: 100%	No	NA	26%
Dols et al. (2010)	1	Yes	The Netherlands	100	2001-2004	47%	52.5	MIDN: 50% LDN: 50%	Related: 74% Unrelated: 26%	Yes	88%	11%
Dols et al. (2014)	1	Yes	The Netherlands	190	2008-2010	52%	52.6	LDN: 50% HARP: 50%	NA	Yes	91%	14%
Frade et al. (2008)	1	Yes	Portugal	32	NA	53%	41 (21-64)	MIDN: 100%	Related: 100%	No	NA	NA
Fukunishi et al. (2002)	2	-	Japan	65	NA	54%	53.1 (31-64)	NA	NA	No	NA	NA
Garcia et al. (2013)	1	Yes	Brazil	50	2007-2009	62%	41 (25-68)	MIDN: 100%	Related: 92% Unrelated: 8%	No	100%	0%
Glotzer et al. (2013)	2	-	USA	83	2000-2010	69%	42.8 (18-60)	NA	NA	No	37%	0%
De Groot et al. (2012)	2	-	The Netherlands	316	1997-2009	65%	52.6 (25-77)	ODN: 0.3% MIDN: 96.7% LDN: 3%	Related: 54% Unrelated: 46%	No	74%	0%
Gross et al. (2013)	2	-	USA	233	1963-2005	61%	58 (24-94)	ODN: 66% LDN: 33% Unknown: 1%	Related: 78% Unrelated: 22%	Yes	73%	0%
Guleria et al. (2011)	1	Yes	India	73	NA	100%	42.6 ± 10.5	MIDN: 84%. LDN: 16%	Related: 100%	No	100%	NA

Table 2. Characteristics of studies included in the systematic review and meta-analysis for both course and prediction of health-related quality of life (continued)

Author (year)	Study Purpose	Course data available for meta-analysis	Country	N	Year data collection	Percent female, %	Donor age (range)	Surgery Technique	Donor type	Multi-center	Response rate	Drop-out last assessment
Klop et al. (2013 - I)	1	No	The Netherlands	501	2001-2010	54%	<40: 20%, 40-60: 53%, 60-70: 21%, 70< 6%	MIDN: 24%, LDN: 57%, HARP:19%	Related: 55% Unrelated: 45%	Yes	NA	16%
Klop et al. (2013 - II)	1	Yes	The Netherlands	40	2011-2012	58%	48.0 (21-77)	LDN: 50% HARP: 50%	NA	No	98%	37%
Kok et al. (2006 - I)	1	Yes	The Netherlands	100	2001-2004	47%	48.8	MIDN: 50% LDN: 50%	Related: 74% Unrelated: 26%	Yes	88%	11%
Kok et al. (2006 - II)	1	No	The Netherlands	100	2001-2005	61%	52.1 (20-90)	MIDN: 45% LDN: 55%	Related: 52%, Unrelated: 48%	No	80%	11%
Kroencke et al. (2012)	1	Yes	Germany	79	2005-2009	61%	53.6 ± 11.3	ODN: 37%, MIDN: 52%, LDN: 11%	Related: 59% Unrelated:41%	No	93%	25%
Kurien et al. (2011)	1	Yes	India	50	2009-2010	70%	45.8	LDN: 50% LESS: 50%	NA	No	NA	NA
Lopes et al. (2011)	1	No	Portugal	45	2002-2008	58%	41.2 (20-60)	MIDN: 100%	Related: 100%	No	100%	60%
Lopes et al. (2013)	1	Yes	Portugal	45	2002-2008	58%	41.2 (20-60)	MIDN: 100%	Related: 100%	No	100%	60%
Lumsdaine et al. (2005)	1	Yes	United Kingdom	40	2000-2004	63%	49 (24-71)	ODN:100%	Related: 65% Unrelated: 35%	Yes	95%	23%
Massey et al. (2010)	1+2	Yes	The Netherlands	24	2000-2008	54%	58.5 (33-84)	LDN: 100%	Unrelated: 100%	No	96%	NA
Minnee et al. (2008)	1	Yes	The Netherlands	105	2002-2006	58%	<35:12%, 35-44: 26%, 45-54:29%, 55-64:26%, 65-74: 6%, >74: 1%	HALN: 100%	Related: 62% Unrelated: 38%	No	100%	2%

Table 2. Characteristics of studies included in the systematic review and meta-analysis for both course and prediction of health-related quality of life (continued)

Author (year)	Study Purpose	Course data available for meta-analysis	Country	N	Year data collection	Percent female, %	Donor age (range)	Surgery Technique	Donor type	Multi-center	Response rate	Drop-out last assessment
Minz et al. (2005)	1	Yes	India	75	2003	72%	42.8 ± 11.6	NA	Related: 75% Unrelated: 25%	No	NA	NA
Nicholson et al. (2011)	1	Yes	United Kingdom	84	2000-2004	60%	46.3	MIDN: 33% LDN: 67%	NA	No	89%	NA
Rodrigue et al. (2013)	2	-	USA	133	2002-2012	57%	43.1 ± 11.2	LDN: 100%	Related: 54% Unrelated: 46%	Yes	92%	16%
Smith et al. (2003)	1	Yes	Australia	48	1997-2001	52%	48 (26-72)	ODN: 100%	Related: 61% Unrelated: 39%	No	98%	8%
Smith et al. (2004)	1+2	Yes	Australia	48	1998-2002	54%	48.7 (26-72)	ODN: 85% LDN 15%	NA	No	94%	6%
Timmerman et al. (2013)	1	Yes	The Netherlands	49	2000-2011	43%	59 (31-84)	LDN: 100%	Unrelated: 100%	No	99%	29%
Vemuru Reddy et al. (2011)	1	Yes	India	106	NA	73%	43.2 (22-65)	MIDN: 86% LDN: 14%	Related:76% Unrelated: 24%	No	94%	6%
Virzi et al. (2007)	1	Yes	Italy	48	2002-2004	79%	54.2 (33-81)	ODN: 100%	Related: 75% Unrelated: 25%	No	NA	NA
Walton-Moss et al. (2007)	1	No	USA	52	NA	67%	41.5 ± 11.8	LDN: 100%	Related: 100%	No	100%	81%

Note. Study purpose 1: HRQoL Course Study, 2: Prediction Study, N: number of donors included, response rate: percentage of donors that agreed to participate, NA: data not reported

HALN: hand-assisted transperitoneal laparoscopic donor nephrectomy, HARP: hand-assisted retroperitoneoscopic donor nephrectomy, LDN: standard laparoscopic donor nephrectomy, LESS: laparo-endoscopic single-site donor nephrectomy, MIDN: mini-incision open donor nephrectomy, ODN: open donor nephrectomy.

Table 3. Meta-analytic results of studies assessing the change in health-related quality of life of living kidney donors at different post-donation assessment periods as compared to pre-donation functioning

Timing postdonation HRQoL assessment	Sample Size		Heterogeneity[3]		Effect sizes			
	k[1]	*n*[2]	I^2 (%)[4]	*p*[5]	SMD[6]	95% CI[7]	*z*[8]	*p*[9]
1-2 months								
Physical Disability	13	625	49	.02	-1.03	[-1.12, -0.93]	20.65	<.001
ODN	3	121	6	.35	-1.20	[-1.44, -0.97]	10.09	<.001
MIDN	2	79	0	.97	-1.26	[-1.55, -0.96]	8.43	<.001
LDN	8	425	54	.03	-0.95	[-1.06, -0.83]	16.12	<.001
Pain	12	588	83	<.001	-1.05	[-1.31, -0.80]	8.16	<.001
ODN	2	83	93	<.001	-1.40	[-2.55, -0.26]	2.40	.02
MIDN	2	79	0	.39	-0.89	[-1.15, -0.63]	6.73	<.001
LDN	8	426	84	<.001	-1.02	[-1.32, -0.71]	6.58	<.001
Fatigue	12	586	49	.03	-0.93	[-1.03, -0.83]	18.69	<.001
ODN	2	81	0	.67	-1.04	[-1.31, -0.77]	7.59	<.001
MIDN	2	79	36	.21	-0.66	[-0.90, -0.42]	5.40	<.001
LDN	8	426	50	.05	-0.97	[-1.09, -0.86]	16.39	<.001
Psychological Functioning	13	626	73	<.001	-0.22	[-0.38, -0.06]	2.72	.007
ODN	3	121	73	.02	-0.38	[-0.75, 0.00]	1.97	.05
MIDN	2	79	0	.56	-0.40	[-0.63, -0.17]	3.37	<.001
LDN	8	426	75	<.001	-0.13	[-0.33, 0.07]	1.27	.20
Social-relational Functioning	13	628	67	<.001	-0.69	[-0.78, -0.61]	15.42	<.001
ODN	3	123	89	<.001	-0.48	[-0.67, -0.28]	4.84	<.001
MIDN	2	79	0	.85	-0.62	[-0.86, -0.37]	4.96	<.001
LDN	8	426	29	.20	-0.78	[-0.89, -0.67]	14.05	<.001
3-6 months								
Physical Disability	14	683	87	<.001	-0.16	[-0.39, 0.07]	1.38	.17
ODN	3	140	76	.02	-0.13	[-0.48, 0.22]	0.73	.46
MIDN	6	360	94	<.001	-0.15	[-0.64, 0.33]	0.63	.53
LDN	5	183	0	.44	-0.17	[-0.31, -0.02]	2.25	.02
Pain	8	345	58	.02	-0.36	[-0.47, -0.25]	6.48	<.001
ODN	1	48	-	-	-0.69	[-1.00, -0.38]	4.31	<.001
MIDN	3	139	61	.08	-0.36	[-0.53, -0.19]	4.13	<.001
LDN	4	158	51	.10	-0.28	[-0.44, -0.12]	3.41	<.001
Fatigue	8	346	82	<.001	-0.22	[-0.49, 0.05]	1.63	.10
ODN	1	48	-	-	0.56	[0.25, 0.87]	3.50	<.001
MIDN	3	139	71	.03	-0.20	[-0.52, 0.13]	1.19	.23
LDN	4	159	0	.65	-0.43	[-0.60, -0.27]	5.27	<.001

Table 3. Meta-analytic results of studies assessing the change in health-related quality of life of living kidney donors at different post-donation assessment periods as compared to pre-donation functioning (continued)

Timing postdonation HRQoL assessment	Sample Size		Heterogeneity[3]		Effect sizes			
	k[1]	*n*[2]	I^2 (%)[4]	*p*[5]	SMD[6]	95% CI[7]	*z*[8]	*p*[9]
Psychological Functioning	15	684	93	<.001	0.18	[-0.10, 0.47]	1.26	.21
ODN	3	140	85	.002	-0.30	[-0.73, 0.13]	1.37	.17
MIDN	6	360	96	<.001	0.35	[-0.22, 0.91]	1.20	.23
LDN	5	184	85	<.001	0.32	[-0.09, 0.73]	1.51	.13
Social-relational Functioning	11	519	80	<.001	0.03	[-0.16, 0.22]	0.34	.73
ODN	1	48	-	-	0.81	[0.48, 1.14]	4.76	<.001
MIDN	5	312	57	.05	-0.02	[-0.20, 0.16]	0.21	.84
LDN	4	159	9	.35	-0.14	[-0.31, 0.03]	1.64	.10
≥12 months								
Physical Disability	15	703	65	<.001	-0.12	[-0.20, -0.05]	3.17	.002
ODN	3	141	60	.08	-0.30	[-0.48, -0.13]	3.46	<.001
MIDN	6	270	80	<.001	-0.13	[-0.25, -0.01]	2.09	.04
LDN	6	292	0	.61	-0.03	[-0.15, 0.08]	0.57	.57
Pain	13	617	0	.50	-0.10	[-0.18, -0.02]	2.54	.01
ODN	2	103	0	.41	-0.24	[-0.44, -0.04]	2.34	.02
MIDN	5	220	0	.82	-0.06	[-0.19, 0.08]	0.84	.40
LDN	6	294	27	.23	-0.09	[-0.21, 0.02]	1.59	.11
Fatigue	13	615	19	.26	-0.26	[-0.35, -0.18]	6.41	<.001
ODN	2	101	13	.28	-0.39	[-0.59, -0.19]	3.83	<.001
MIDN	5	220	15	.32	-0.19	[-0.32, -0.05]	2.76	.006
LDN	6	294	18	.30	-0.28	[-0.40, -0.16]	4.64	<.001
Psychological Functioning	17	778	49	.01	-0.11	[-0.18, -0.04]	2.95	.003
ODN	3	141	0	.42	-0.24	[-0.41, -0.07]	2.76	.006
MIDN	6	270	56	.05	-0.08	[-0.20, 0.04]	1.27	.21
LDN	8	367	54	.03	-0.08	[-0.18, 0.03]	1.49	.14
Social-relational Functioning	16	730	35	.09	.04	[-0.03, 0.12]	1.17	.24
ODN	3	143	3	.35	-0.13	[-0.30, 0.04]	1.50	0.13
MIDN	5	220	44	.13	0.14	[0.00, 0.28]	1.99	0.05
LDN	8	367	10	.35	0.05	[-0.05, 0.15]	1.03	0.30

HRQoL, health-related quality of life; LDN, laparoscopic donor nephrectomy; MIDN, mini-incision donor nephrectomy; ODN, open donor nephrectomy.

*Estimated correlation between pre-donation and post-donation assessment of HRQoL was 0.5

[1] number of comparisons, [2] number of donors included in analysis, [3] the variation in study outcomes between studies, [4] the percentage of variation across studies that is due to heterogeneity rather than chance, [5] significance level of heterogeneity, [6] standardized mean difference pre-donation vs. post-donation (Effect Size), [7] Confidence Interval, [8] Test for overall effect, [9] significance level of effect assessment

Physical functioning

Physical disability

During the first 2 months after donation, physical disability was higher than at baseline, with a large ES (-1.03 [95% confidence interval (CI) -1.12 to -0.93]) (9,12,14,47-53). At 3-6 months after donation, physical disability was comparable to baseline (small ES -0.16 [95% CI -0.39 to 0.07]) (2,3,11,23,49-52,54-58); however, long-term physical disability was higher again (small ES -0.12 [95% CI -0.20 to -0.05]) (2,3,9,10,14,23,46,48,49,51,53,59) (see forest plot in Figure S3). Clinically significant changes between pre- and post-donation assessments were found during the early postoperative recovery period in all studies but in only 17% of studies long term. Long-term physical disability was comparable to general population norms.

Pain

During all post-donation periods, higher pain levels were found than at baseline, with a large ES during the first two post-donation months, and small ESs at the other assessments (ES range: -1.05 to -0.10 [95% CI range (-1.31 to -0.80) to (-0.18 to -0.02)]) (2,3,9,10,12,14,46,47,49-53,55,56,59) (Figure S4). Clinically significant changes between pre- and post-donation assessments were found in the early postoperative recovery period in all studies but in only 20% of studies long term. Pain levels long term were comparable to general population norms.

Fatigue

During the first 2 months after donation, higher fatigue levels were found than at baseline, with a large ES (-0.93 [95% CI -1.03 to -0.83]) (9,12,14,47,49-53). At 3-6 months after donation, fatigue was comparable to baseline (-0.22 [95% CI -0.49 to 0.05]) (3,49-52,55,56); however, long-term fatigue was higher again (small ES -0.26 [95% CI -0.35 to -0.18]) (2,3,9,10,14,46,49,51,53,59) (Figure S5). Clinically significant changes between pre- and post-donation assessments were found in the early postoperative recovery period in all studies and in 50% of studies long term after donation; however, long-term fatigue levels were also comparable to general population norms.

Psychological functioning

During the first 2 months after donation, psychological functioning was reduced in comparison to that before donation (small ES -0.22 [95% CI -0.38 to -0.06]) (9,12,14,47-53). At 3-6 months after donation, psychological functioning was comparable to baseline (ES 0.18 [95% CI -0.10 to 0.47]) (2,3,11,23,49-52,54-58,60). Long-term psychological functioning was reduced again (small ES -0.11 [95% CI -0.18 to -0.04]) (2,3,9,10,14,23,46,48,49,51,53,59,61,62) (Figure S6). Clinically significant changes between pre- and post-donation assessments were found in 50% of studies during the early recovery period

and in 7% of studies long term after donation. Long-term psychological functioning was comparable to general population norms.

Social-relational functioning

During the first 2 months after donation, social-relational functioning was reduced compared with baseline, with a moderate ES (-0.69 [95% CI -0.78 to -0.61]) (9,12,14,47-53), but similar to baseline for the later periods (ES 0.03 [95% CI -0.16 to 0.22] and 0.04 [95% CI -0.03 to 0.12], respectively) (2,3,9,10,14,46,48-53,55-62) (Figure S7). Clinically significant differences were found during the early postoperative recovery period in 90% of studies but in only 8% of studies long term after donation. Long-term social functioning was comparable to that of the general population.

In summary, results show that shortly after donation, as expected, donors have a HRQoL reduction in comparison to the level before donation, with small to moderate ESs for psychological and social functioning and large ESs for physical functioning, with scores that correspond with norms for clinically relevant changes. In the short term, HRQoL returned to baseline on all domains except pain, which was still slightly reduced (small ES). In the long term, donors on average showed somewhat reduced physical and psychological functioning compared with functioning before donation (small ES), but levels were comparable to general population norms, and differences between pre-and post-donation assessments were not clinically relevant. In the longer term, slightly elevated scores of fatigue were found in 50% of studies, but fatigue scores were still comparable to general population norms. The individual results of studies that had to be excluded due to missing data were overall in the same line (see Table S1).

Secondary analyses

Subgroup analyses were conducted to study differences in pre- and post-donation HRQoL changes for different surgery techniques. Results were generally comparable for the different surgery techniques, with a few exceptions that did not show a consistent pattern of better or worse functioning for one surgery technique compared with others (Table 3).

Because of the heterogeneity between studies, sensitivity analyses were conducted on the use of different questionnaires within one HRQoL domain and study quality assessment. Studies could not be compared with regard to applying more or less stringent donor eligibility criteria because these criteria were not reported in most studies. Results were mainly robust across the use of different questionnaires and study quality. Finally, HRQoL outcomes were similar for imputing low (r=0.1) or high (r=0.9) correlation coefficients instead of the average (r=0.5) correlation coefficients between pre- and post-donation assessments.

Table 4. Physical and psychological predictors of longer-term HRQoL of living kidney donors

Source	Predictors	Psychosocial outcome assessment		Physical outcome assessment	
		Outcome	***p***	**Outcome**	***p***
Bahler et al. (2013)	**Physical:**	SF36 MCS 1 month post-donation			
	• pre-donation BMI		NS		
	• nephrectomy side		NS		
	• use of a hand-assistance port		NS		
	• surgery duration		NS		
	• length of hospital stay		NS		
	Psychological:				
	• psychiatric history		<.05		
	Social-relational:				
	• relation to the recipient		NS		
	• recipient complications		<.05		
	Other:				
	• age		NS		
	• female gender		<.05		
	• marital status		NS		
Chien et al. (2010)	**Physical:**	Change in SF36 MH before-3 months post-donation			
	• pre-donation body weight		NS		
	• pre-donation BMI		NS		
	• serum creatinine 2 days post-donation		NS		
	• 24h creatinine clearance		<.01		
	• hospital stay		NS		
	Social-relational:				
	• relationship with recipient		NS		
	Other:				
	• age		NS		
	• gender		NS		
Fukunishi et al. (2002)	**Psychological:**	Post-donation psychiatric syndrome			
	• pre-donation alexithymia		NS		
Glotzer et al. (2013)	**Physical:**	SF36 MCS post-donation		SF36 PCS post-donation	
	• pre-donation BMI		NS		NS
	• pre-donation creatinine level		NS		NS
	Other:				
	• age		NS		NS
de Groot et al. (2012)	**Physical:**	SF36 MCS post-donation		SF36 PCS post-donation	
	• pre-donation BMI		NS		NS
	• pre-donation smoking		NS		<.01
	• pre-donation blood pressure		NS		NS
	• pre-donation renal clearance		NS		NS
	• pre-donation cardiovascular events		NS		NS
Gross et al. (2013)	**Physical:**	SF36 MCS post-donation		SF36 PCS post-donation	
	• pre-donation BMI -		NS		<.001
	Psychological:				
	• history of psychiatric difficulties -		<.001		<.001

Table 4. Physical and psychological predictors of longer-term HRQoL of living kidney donors (continued)

Source	Predictors	Psychosocial outcome assessment		Physical outcome assessment	
		Outcome	***p***	**Outcome**	***p***
	Other:				
	• age +		<.001		NS
	• non-white race		NS		<.01
Massey et al. (2010)	**Physical:**	Satisfaction with donation			
	• self-rated health scores	post-donation	NS		
	Psychological:				
	• inadequacy in thought and action		<.05		
	• mental health history		NS		
	Physical:	Perceived impact of donation on psychological well-being post-donation			
	• self-rated health scores		NS		
	Psychological:				
	• pre-donation psychological complaints		NS		
	• mental health history		NS		
	Psychological:	Worse satisfaction with supervision during admittance to the hospital post-donation			
	• pre-donation phobic anxiety		<.05		
	• pre-donation depression		<.05		
	• pre-donation hostility		<.01		
Rodrigue et al. (2013)	**Social-relational:**	Overestimation expectancies of:			
	• recipient graft failure	• personal growth	<.05		
		• interpersonal benefit	NS		
		• spiritual growth	NS		
Smith et al. (2004)	**Physical:**	Psychiatric caseness 12 months post-donation			
	• surgery technique		NS		
	• length of hospital stay		NS		
	• pre-donation SF36 PCS		NS		
	• SF36 PCS 4 months post-donation		<.01		
	Psychological:				
	• psychiatric caseness lifetime		NS		
	• psychiatric caseness previous 12 months		NS		
	• pre-donation SF36 MCS		<.05		
	• SF36 MCS 4 months post-donation		<.01		
	• psychiatric caseness 4 months post-donation		<.01		
	Social-relational:				
	• recipient hospital stay		NS		
	• recipient graft failure		NS		
	• donor-recipient relationship		NS		
	Other:				
	• age		NS		
	• gender		NS		
	• marital status		NS		

Table 4. Physical and psychological predictors of longer-term HRQoL of living kidney donors (continued)

Source	Predictors	Psychosocial outcome assessment		Physical outcome assessment	
		Outcome	*p*	Outcome	*p*
	Physical:	SF36 MCS 12 months postoperatively			
	• surgery technique		NS		
	Psychological:				
	• pre-donation TERS scores -		<.05		
	• SF36 MCS 4 months post-donation +		<.01		

- negative correlation coefficient, + positive correlation coefficient, NS not significant.
BMI: Body Mass Index, SF36 MCS: Short Form-36 Mental Component Summary Score, SF36 PCS: Short Form-36 Physical Component Summary Score, TERS: Transplant Evaluation Rating Scale.

Prediction of HRQoL

Nine studies investigated pre- or post-donation predictors for long-term HRQoL after kidney donation, with each predictor being included in up to five studies at most (Table 4). Reduced post-donation physical functioning was related to non-white race (63), smoking (21) and a history of psychiatric difficulties (63), whereas it was not related to age (63,64), pre-donation creatinine levels (21,64), blood pressure and cardiovascular events (21). Inconsistent results were found for BMI, which was related to physical functioning in one (63) of three studies (21,63,64).

Reduced post-donation psychological functioning was related to worse self-reported physical functioning 4 months after donation and to worse psychological functioning before and 4 months after donation (2). Reduced psychological functioning was not related to pre-donation self-rated health (61), marital status (2,52), non-white race (63), pre-donation BMI (21,52,56,63,64), creatinine level (64), smoking, blood pressure, cardiovascular events (21), surgery technique (2,52) or duration (52), nephrectomy side, use of a hand-assistance port (52), length of hospital stay (2), inability to distinguish and verbalize emotions (alexithymia) (65), the donor-recipient relationship or recipient length of hospital stay (2,52,56). Inconsistent results were found for recipient complications (related in two [52,66] of three studies [2,52,66]), lower age (related in one [63] of five studies [2,52,56,63,64]), female sex (related in one [52] of three studies [2,52,56]) and psychiatric history (related in two [52,63] of four studies [2,52,61,63]). No predictors were examined for post-donation social-relational functioning.

DISCUSSION

This systematic review and meta-analysis investigated prospective studies on the course and predictors of HRQoL (i.e., physical, psychological and social-relational functioning) after living kidney donation. Results indicated that shortly after donation, donors have

lower HRQoL than before donation on all domains, with small to moderate changes in psychological and social functioning and large changes in physical functioning. At 3-12 months after donation, HRQoL returned to baseline or was slightly reduced compared with that before donation, particularly for fatigue; however, levels were comparable to those of the general population. Results were mainly robust across surgery techniques, questionnaires used and study quality. The limited number of prediction studies have provided only some rudimentary ideas on potential risk factors for developing longer-term HRQoL problems; however, results indicated that donors with low psychological functioning at baseline were those most at risk of impaired longer-term HRQoL.

The current review extended the findings from the 2006 review on psychosocial HRQoL (5) by distinguishing different HRQoL domains, using quantifiable meta-analytic techniques, addressing the influence of surgery techniques and methodological bias, and including the prospective results of recent and large cohort studies. Results of the current meta-analysis were generally in line with the previous review, showing that HRQoL was comparable with general population norms during the long-term post-donation period, with slightly reduced scores for physical and psychological functioning (5).

The short-term reduction of post-donation physical HRQoL is not unexpected because of the invasive surgical intervention performed in a healthy body. Previous research indicated that donors experienced more postoperative pain than expected before surgery (67-69), and this underscores the importance of providing appropriate pre-surgery information about possible short-term and long-term health outcomes. The invasive surgery and resulting short-term physical disabilities may explain, at least in part, the early reduction of psychological and social-relational functioning, which could also be the result of psychological factors (e.g., anxiety) and social-relational factors (e.g., concerns about the recipient's health) (5).

The results of the current meta-analysis can support guidelines for future donor decision making, which can be used in donor counselling in clinical practice. Clinicians can inform potential donors that although HRQoL scores decrease shortly after donation, HRQoL recovers to population norms within several months after donation. Only fatigue scores could remain somewhat higher in the long term, but findings are also comparable to general population norms. The possible continuation of higher fatigue levels long term is a new finding that requires further investigation. It is not yet clear whether these findings might be a consequence of donation; however, it could potentially be the consequence of a combination of multiple factors (e.g., aging, living with one kidney, or because donors are not familiar with physical limitations and may be inclined to resume their daily activities too early after surgery). Although fatigue has been found to correlate with worse psychological functioning in the general population (34,70) and in patients with chronic somatic conditions (71,72), the comparison of donors' HRQoL with general population norms in this meta-analysis indicated that post-donation HRQoL

scores were comparable to the general population for all dimensions. The description of a valid comparison group remains important in future donor research.

From the limited and inconclusive results on prospective predictors of long-term HRQoL, no firm conclusions can be drawn, but the most consistent evidence points to low psychological functioning as a predictor for impaired long-term HRQoL and underscores the relevance of screening of psychological functioning and psychiatric history. Consequently, additional counselling might be beneficial for donors with HRQoL scores that differ from general population norms in terms of clinically relevant differences; however, this systematic review clearly indicates that more prospective research in sufficiently sized samples is required to identify relevant HRQoL risk factors at an early stage that may be used to develop and offer interventions to prevent longer-term HRQoL problems in living kidney donors.

A number of studies could not be included because of methodological constraints, such as recall bias, and because only generic HRQoL scores were provided. Moreover, the studies that were included had some limitations. First, the impact of the currently applied, more liberal criteria for donor selection on post-donation HRQoL could not be examined because studies did not clearly distinguish between the use of strict versus more lenient donor eligibility criteria. Second, the timing of pre-donation assessments varied from months to a few days before surgery, with 55% of studies not specifying the timing of the pre-donation assessment, making it difficult to compare baseline findings and preventing the assessment of the impact of timing on HRQoL changes. Because pre-donation assessments are often part of the donor selection procedure, elevated pre-donation HRQoL scores could be reported out of fear not to pass the screening procedure when problems would be reported. In contrast, pre-donation assessments a few days before surgery may lead to higher-than-normal distress levels because of the upcoming surgery. Third, although response rates for first assessments were generally high, response rates for repeated assessments were often not reported and may have affected the results. Fourth, some potentially relevant predictors of post-donation HRQoL have not been examined yet, including donor complications during or after surgery, the donor-recipient relationship type (e.g., directed versus non-directed donation), more lenient eligibility criteria for donors, cultural differences (e.g., with regard to health care systems and screening procedures), recipient and graft survival, and pre-transplant health status of the recipient (e.g., on dialysis or not). Finally, although it cannot be totally excluded that the results after donation are possibly influenced by the phenomenon of regression to the mean (73,74), this seems unlikely because repeated measures of HRQoL after donation do not show a consistent decrease in HRQoL scores over time, and the large number of studies included did not show a similar regression to the mean individually.

In conclusion, this systematic review and meta-analysis showed that HRQoL returned to baseline or was only slightly reduced on longer-term assessments, although HRQoL scores decreased shortly after donation; however, HRQoL levels were comparable to general population norms. On the basis of these results, clinicians can inform potential donors that there is generally no risk involved with the donation. Results of prediction studies indicate that donors with low psychological functioning at baseline are those most at risk of impaired long-term HRQoL.

Future research is required to quantify the extent and identify the reasons for the small reduction of long-term HRQoL to estimate the need for future interventions for this group. Pre-donation psychological functioning was the most consistent predictor for long-term HRQoL after living kidney donation. However, more systematic prospective research on predictors of the HRQoL of living kidney donors is required to identify possible risk factors for longer-term HRQoL problems more reliably. This knowledge could provide valid selection criteria in the psychosocial screening of living kidney donors and could be used to focus psychosocial interventions before and after donation on donors at risk of developing long-term HRQoL problems.

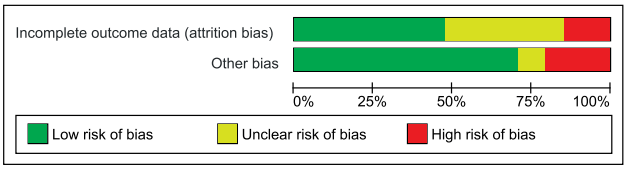


Figure S1. Risk of bias graph. Review authors' judgments about each risk of bias item presented as percentages across all included studies

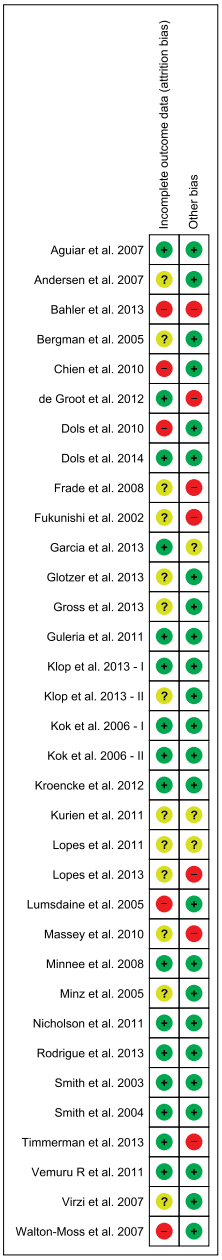


Figure S2. Risk of bias summary. Review authors' judgments about each risk of bias item for each included study.

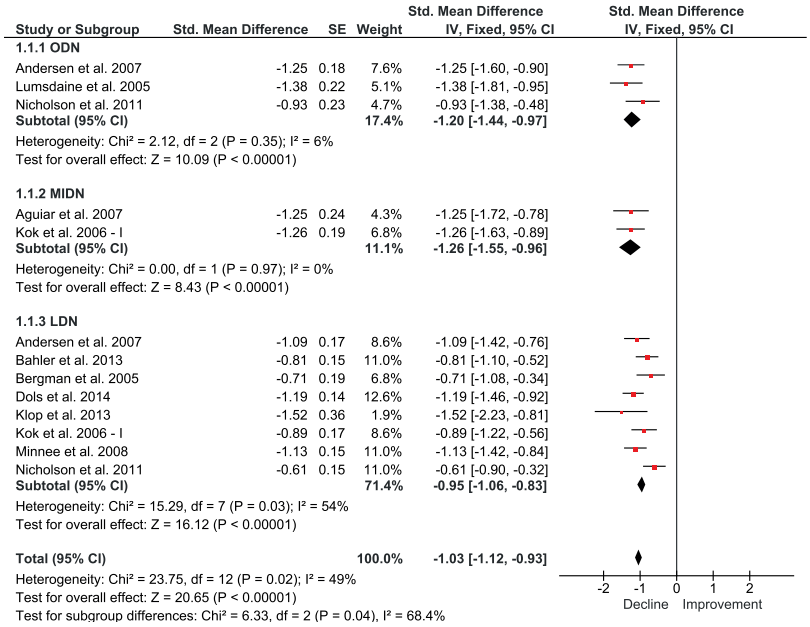


Figure S3a. Forest Plot of the standardized mean difference of changes in physical functioning pre-donation to 1-2 months after donation.

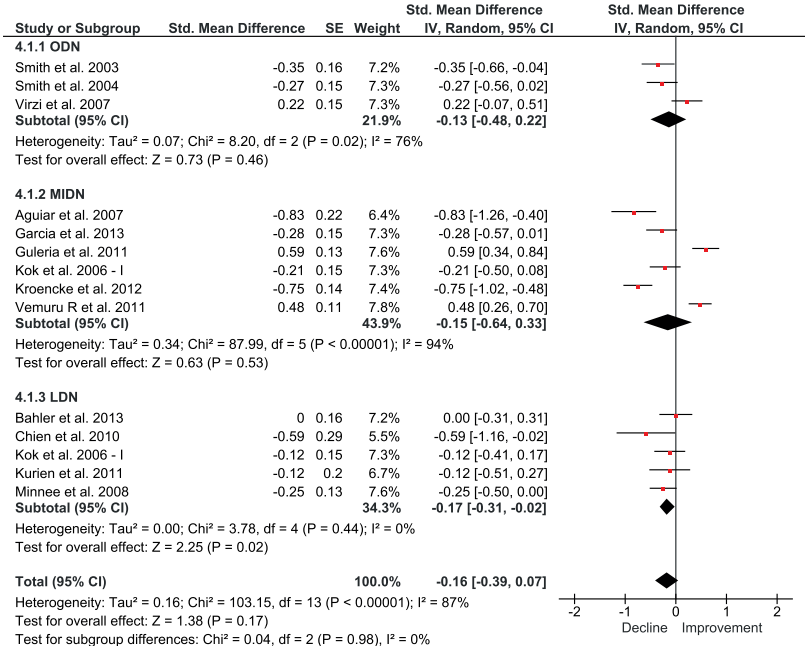


Figure S3b. Forest Plot of the standardized mean difference of changes in physical functioning pre-donation to 3-6 months after donation.

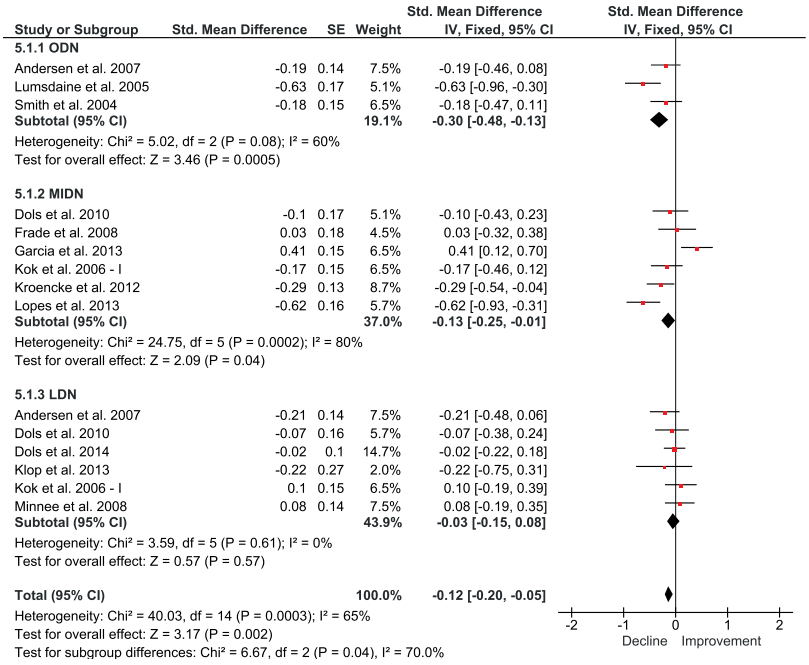


Figure S3c. Forest Plot of the standardized mean difference of changes in physical functioning pre-donation to 12 months or more after donation.

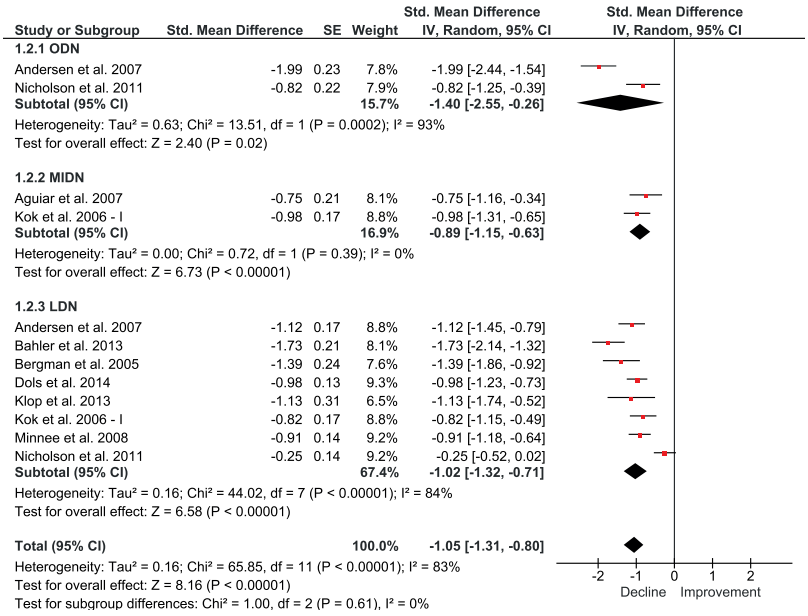


Figure S4a. Forest Plot of the standardized mean difference of changes in pain pre-donation to 1-2 months after donation.

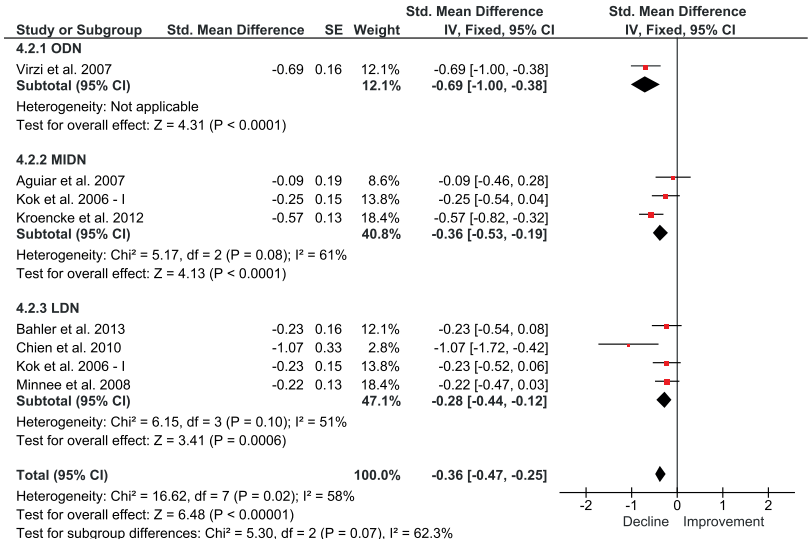


Figure S4b. Forest Plot of the standardized mean difference of changes in pain pre-donation to 3-6 months after donation.

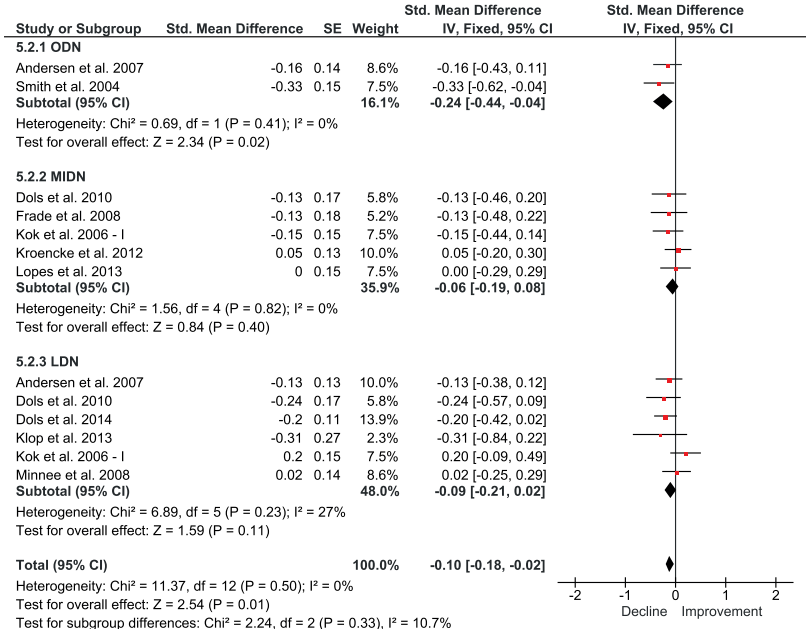


Figure S4c. Forest Plot of the standardized mean difference of changes in pain pre-donation to 12 months or more after donation.

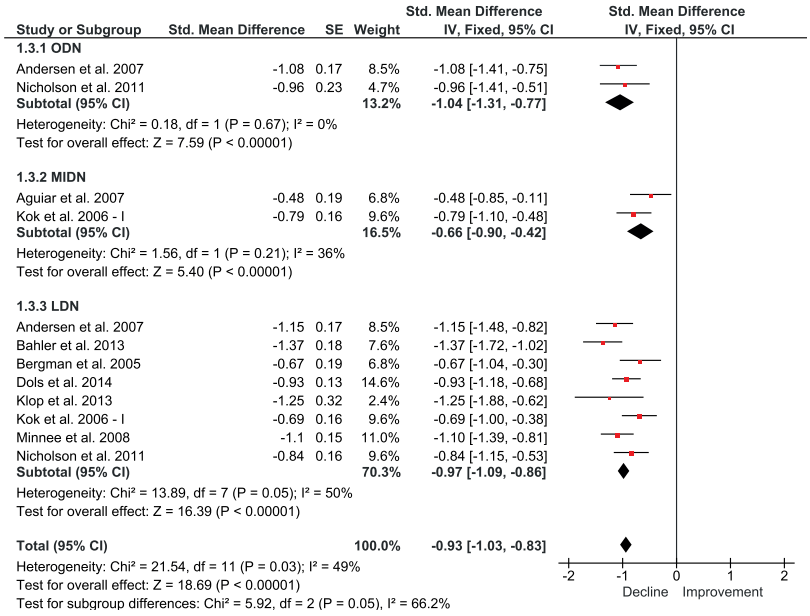


Figure S5a. Forest Plot of the standardized mean difference of changes in fatigue pre-donation to 1-2 months after donation.

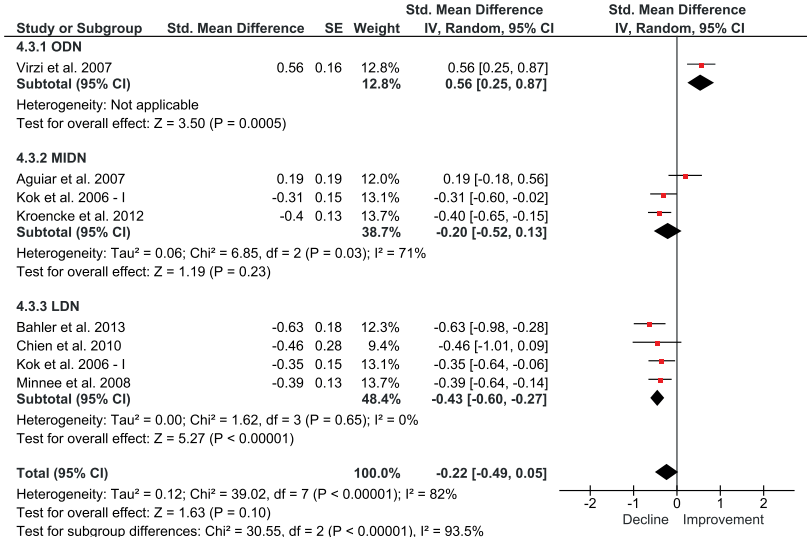


Figure S5b. Forest Plot of the standardized mean difference of changes in fatigue pre-donation to 3-6 months after donation.

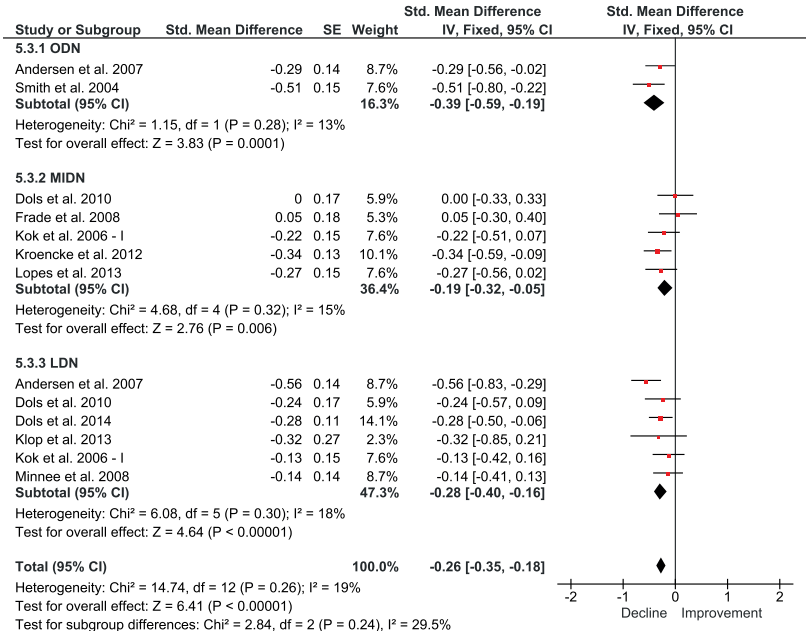


Figure S5c. Forest Plot of the standardized mean difference of changes in fatigue pre-donation to 12 months or more after donation.

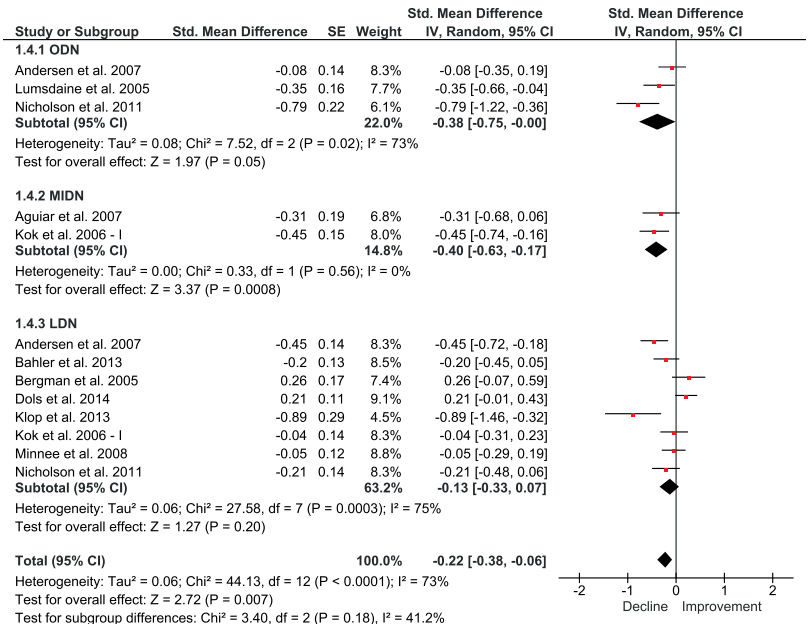


Figure S6a. Forest Plot of the standardized mean difference of changes in psychological functioning pre-donation to 1-2 months after donation.

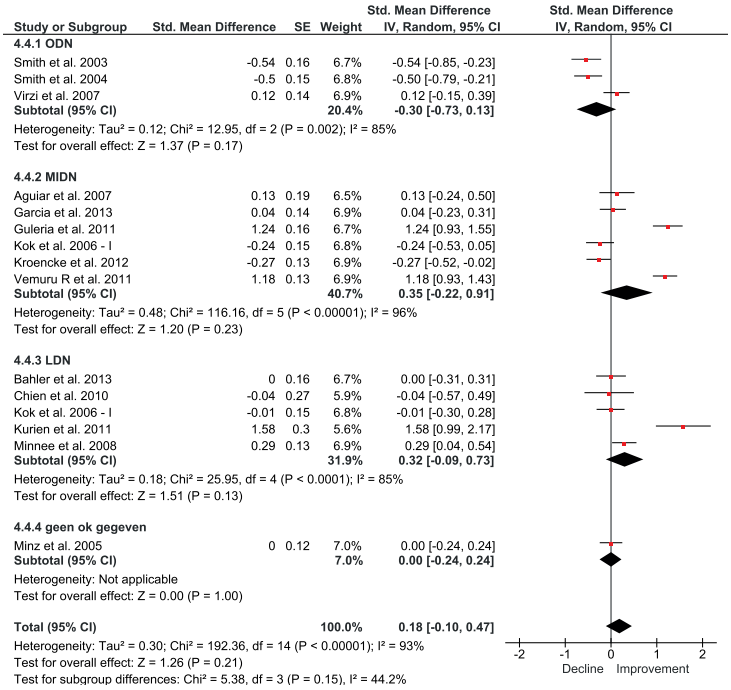


Figure S6b. Forest Plot of the standardized mean difference of changes in psychological functioning pre-donation to 3-6 months after donation.

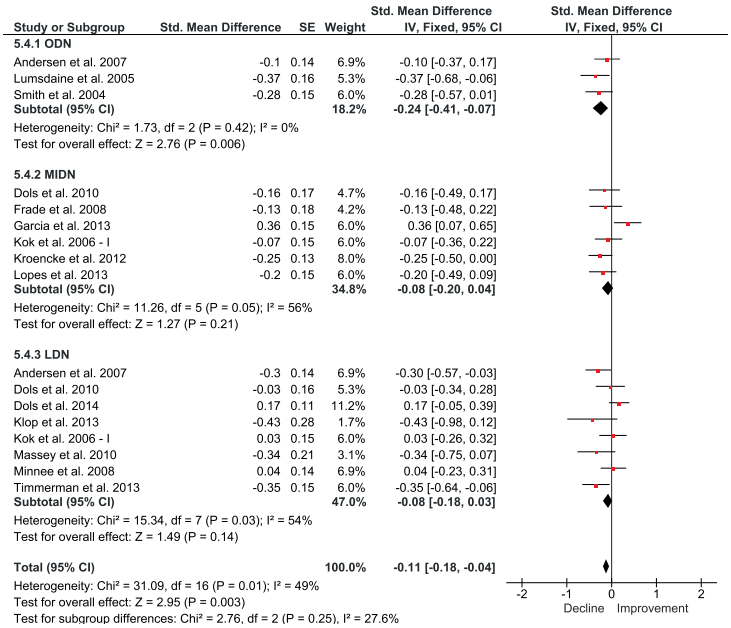


Figure S6c. Forest Plot of the standardized mean difference of changes in psychological functioning pre-donation to 12 months or more after donation.

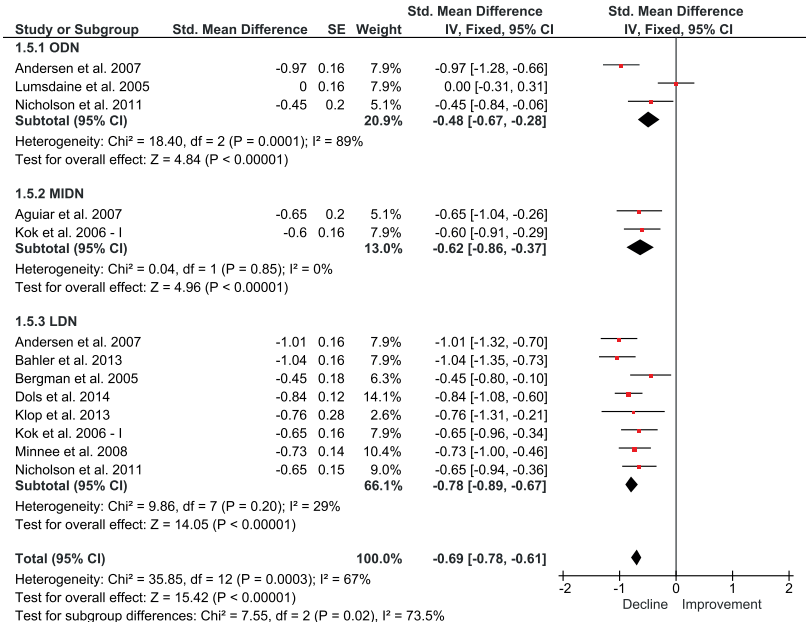


Figure S7a. Forest Plot of the standardized mean difference of changes in social-relational functioning pre-donation to 1-2 months after donation.

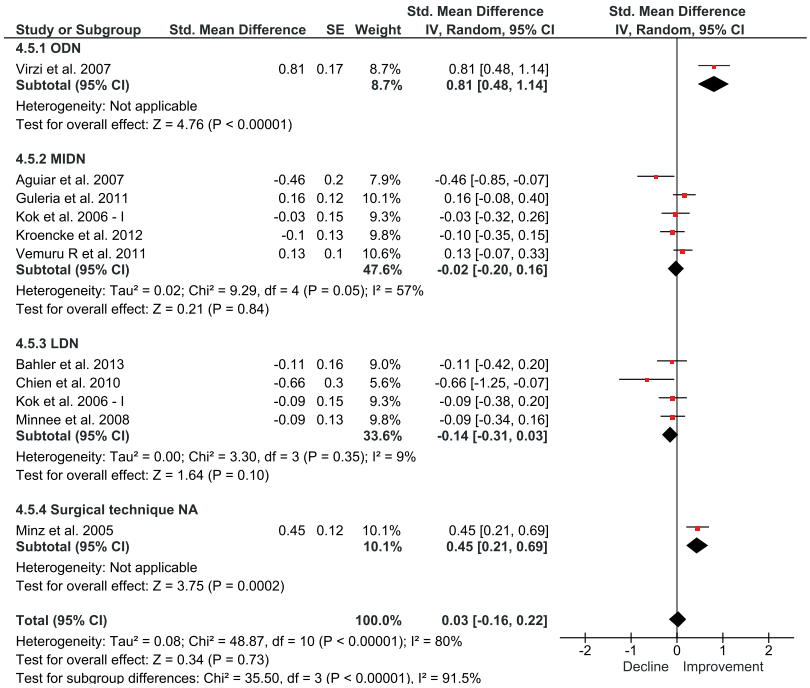


Figure S7b. Forest Plot of the standardized mean difference of changes in social-relational functioning pre-donation to 3-6 months after donation.

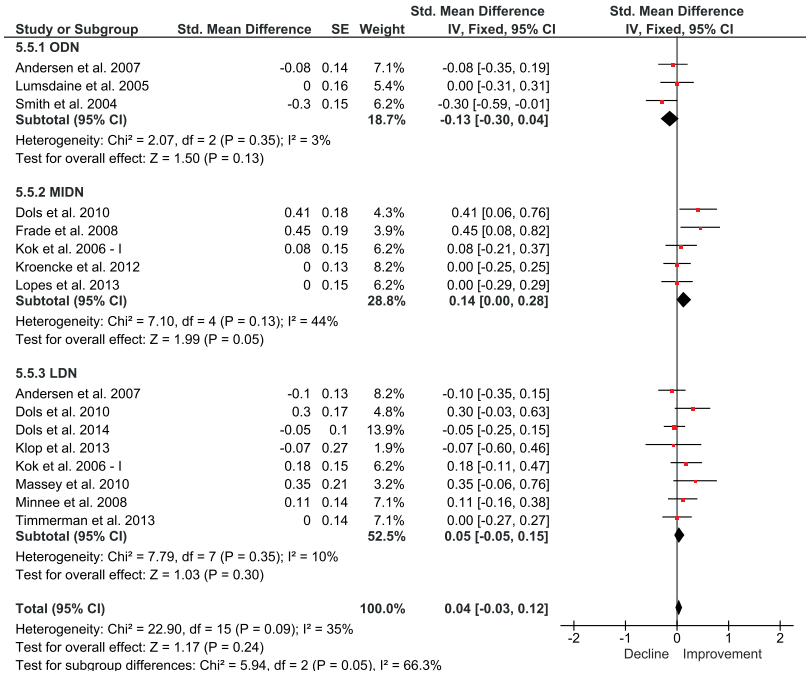


Figure S7c. Forest Plot of the standardized mean difference of changes in social-relational functioning pre-donation to 12 months or more after donation.

Table S1. The course of HRQoL of living kidney donors; studies that could not be included in the meta-analysis

Author	Surgical technique	Postdonation assessment	Physical			Psychosocial	
			Physical disability	Pain	Fatigue	Mental health	Social functioning
Dols et al. (2014)	LDN: 50%	1 month	↓ (p<.05)(PF SF36)	↓ (p<.05)(BP SF36)	↓ (p<.05)(VT SF36)	↑ (p<.05)(MH SF36)	↓ (p<.05)(SF SF36)
		3 months	= (PF SF36)	↓ (p<.05)(BP SF36)	↓ (p<.05)(VT SF36)	↑ (p<.05)(MH SF36)	↓ (p<.05)(SF SF36)
		6 months	= (PF SF36)	= (BP SF36)	↓ (p<.05)(VT SF36)	↑ (p<.05)(MH SF36)	= (SF SF36)
		12 months	= (PF SF36)	= (BP SF36)	↓ (p<.05)(VT SF36)	↑ (p<.05)(MH SF36)	= (SF SF36)
	HARP: 50%	1 month	↓ (p<.05)(PF SF36)	↓ (p<.05)(BP SF36)	↓ (p<.05)(VT SF36)	↑ (p<.05)(MH SF36)	↓ (p<.05)(SF SF36)
		3 months	= (PF SF36)	= (BP SF36)	= (VT SF36)	↑ (p<.05)(MH SF36)	= (SF SF36)
		6 months	= (PF SF36)	= (BP SF36)	= (VT SF36)	↑ (p<.05)(MH SF36)	= (SF SF36)
		12 months	= (PF SF36)	= (BP SF36)	= (VT SF36)	↑ (p<.05)(MH SF36)	= (SF SF36)
Klop et al. (2013)	MIDN: 24%, LDN: 57%, HARP:19%	1 month	↓ (p<.05) (PF SF36)	↓ (p<.05) (BP SF36)	↓ (p<.05) (VT SF36)	↑ (p=.004) (MH SF36)	↓ (p<.05) (SF SF36)
		3 months	↓ (p<.05) (PF SF36)	↓ (p<.05) (BP SF36)	↓ (p<.05) (VT SF36)	↑ (p<.05) (MH SF36)	↓ (p<.05) (SF SF36)
		6 months	↓ (p<.05) (PF SF36)	↓ (p<.05) (BP SF36)	↓ (p<.05) (VT SF36)	↑ (p<.05) (MH SF36)	= (SF SF36)
		12 months	= (PF SF36)	↓ (p<.05) (BP SF36)	↓ (p<.05) (VT SF36)	↑ (p<.05) (MH SF36)	= (SF SF36)

Table S1. The course of HRQoL of living kidney donors; studies that could not be included in the meta-analysis (continued)

Author	Surgical technique	Postdonation assessment	Physical			Psychosocial	
			Physical disability	Pain	Fatigue	Mental health	Social functioning
Kok et al. (2006)	MIDN: 45%	1 month	↓ (p <.03) (PF SF36)	↓ (p <.03) (BP SF36)	↓ (p <.03) (VT SF36) ↓ (p<.001) (MFI20)	↓ (p <.03) (MH SF36)	↓ (p <.03) (SF SF36)
		3 months	= (PF SF36)	↓(p=.02) (BP SF36)	↓(p=.02) (VT SF36) ↓ (p<.001) (MFI20)	= (MH SF36)	= (SF SF36)
		6 months	= (PF SF36)	↓(p=.03) (BP SF36)	= (VT SF36) ↓ (p<.001) (MFI20)	= (MH SF36)	= (SF SF36)
		12 months	= (PF SF36)	= (BP SF36)	= (VT SF36) ↓ (p<.03) (MFI20)	= (MH SF36)	= (SF SF36)
	LDN: 55%	1 month	↓ (p<.002) (PF SF36)	↓ (p<.002) (BP SF36)	↓ (p<.002) (VT SF36) ↓ (p<.05) (MFI20)	↓ (p<.002) (MH SF36)	↓ (p<.002) (SF SF36)
		3 months	= (PF SF36)	= (BP SF36)	↓ (p=.04) (VT SF36) ↓ (p<.02) (MFI20)	= (MH SF36)	= (SF SF36)
		6 months	= (PF SF36)	= (BP SF36)	= (VT SF36) ↓ (p<.02) (MFI20)	= (MH SF36)	= (SF SF36)
		12 months	= (PF SF36)	= (BP SF36)	= (VT SF36) ↓ (p<.02) (MFI20)	= (MH SF36)	= (SF SF36)
Lopes et al (2011)	MIDN: 100%	≥ 1 year				= (SAS) = (SDS)	

REFERENCES

1. WHOQOL: Measuring quality of life. Geneva, Switzerland: World Health Organization; 1997. http://www.who.int/mental_health/media/68.pdf.
2. Smith GC, Trauer T, Kerr PG, Chadban SJ. Prospective psychosocial monitoring of living kidney donors using the Short Form-36 Health Survey: Results at 12 months. Transplantation. 2004; 78: 1384–1389.
3. Kroencke S, Fischer L, Nashan B, Herich L, Schulz KH. A prospective study on living related kidney donors' quality of life in the first year: Choosing appropriate reference data. Clin Transplant. 2012; 26: 418–427.
4. Klop KW, Dols LF, Weimar W, Dooper IM, Ijzermans JN, Kok NF. Quality of life of elderly live kidney donors. Transplantation. 2013; 96: 644–648.
5. Clemens KK, Thiessen-Philbrook H, Parikh CR, et al. Psychosocial health of living kidney donors: A systematic review. Am J Transplant. 2006; 6: 2965–2977.
6. Reimer J, Rensing A, Haasen C, Philipp T, Pietruck F, Franke GH. The impact of living-related kidney transplantation on the donor's life. Transplantation. 2006; 81: 1268–1273.
7. Wiedebusch S, Reiermann S, Steinke C, et al. Quality of life, coping, and mental health status after living kidney donation. Transplant Proc. 2009; 41: 1483–1488.
8. Bargman V, Sundaram CP, Bernie J, Goggins W. Randomized trial of laparoscopic donor nephrectomy with and without hand assistance. J Endourol. 2006; 20: 717–722.
9. Andersen MH, Mathisen L, Veenstra M, et al. Quality of life after randomization to laparoscopic versus open living donor nephrectomy: Long-term follow-up. Transplantation. 2007; 84: 64–69.
10. Dols LFC, Ijzermans JNM, Wentink N, et al. Long-term follow-up of a randomized trial comparing laparoscopic and mini-incision open live donor nephrectomy. Am J Transplant. 2010; 10: 2481–2487.
11. Kurien A, Rajapurkar S, Sinha L, et al. First prize: Standard laparoscopic donor nephrectomy versus laparoendoscopic singlesite donor nephrectomy: A randomized comparative study. J Endourol. 2011; 25: 365–370.
12. Nicholson ML, Elwell R, Kaushik M, Bagul A, Hosgood SA. Health-related quality of life after living donor nephrectomy: A randomized controlled trial of laparoscopic versus open nephrectomy. Transplantation. 2011; 91: 457–461.
13. Hofker HS, Nijboer WN, Niesing J, et al. A randomized clinical trial of living donor nephrectomy: A plea for a differentiated appraisal of mini-open muscle splitting incision and hand-assisted laparoscopic donor nephrectomy. Transpl Int. 2012; 25: 976–986.
14. Dols LF, Kok NF, d'Ancona FC, et al. Randomized controlled trial comparing hand-assisted retroperitoneoscopic versus standard laparoscopic donor nephrectomy. Transplantation. 2014; 97: 161–167.
15. Mandelbrot DA, Pavlakis M, Danovitch GM, et al. The medical evaluation of living kidney donors: A survey of US transplant centers. Am J Transplant. 2007; 7: 2333–2343.
16. Kaisar MO, Nicol DL, Hawley CM, et al. Change in live donor characteristics over the last 25 years: A single centre experience. Nephrology. 2008; 13: 646–650.
17. Wilson CH, Sanni A, Rix DA, Soomro NA. Laparoscopic versus open nephrectomy for live kidney donors. Cochrane Database Syst Rev. 2011: CD006124.
18. Lopes A, Frade IC, Teixeira L, et al. Depression and anxiety in living kidney donation: Evaluation of donors and recipients. Transplant Proc. 2011; 43: 131–136.

19. Tong A, Chapman JR, Wong G, De Bruijn J, Craig JC. Screening and follow-up of living kidney donors: A systematic review of clinical practice guidelines. Transplantation. 2011; 92: 962–972.
20. Andrews PA, Burnapp L, Manas D, et al. Summary of the British Transplantation Society/Renal Association U.K. guidelines for living donor kidney transplantation. Transplantation. 2012; 93: 666–673.
21. De Groot IB, Stiggelbout AM, Van Der Boog PJM, Baranski AG, Marang-Van De Mheen PJ. Reduced quality of life in living kidney donors: Association with fatigue, societal participation and predonation variables. Transpl Int. 2012; 25: 967–975.
22. Duerinckx N, Timmerman L, Van Gogh J, et al. Predonation psychosocial evaluation of living kidney and liver donor candidates: A systematic literature review. Transpl Int. 2014; 27: 2–18.
23. Garcia MFFM, Andrade LGM, Carvalho MFC. Living kidney donors-a prospective study of quality of life before and after kidney donation. Clin Transplant. 2013; 27: 9–14.
24. Higgings JPT, Green S, eds. Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011]. The Cochrane Collaboration. 2011. http://handbook.cochrane.org.
25. Cohen J. Statistical power analysis for the behavioral sciences, 2nd ed. London, UK: Routledge; 1988.
26. Walton-Moss B, Boulware LE, Cooper M, Taylor L, Dane K, Nolan MT. Prospective pilot study of living kidney donor decision-making and outcomes. Clin Transplant. 2007; 21: 86–93.
27. Kok NFM, Alwayn IPJ, Tran KTC, Hop WCJ, Weimar W, Ijzermans JNM. Psychosocial and physical impairment after mini-incision open and laparoscopic donor nephrectomy: A prospective study. Transplantation. 2006; 82: 1291–1297.
28. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986; 7: 177–188.
29. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre TCC, 2014. Version 53 Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.
30. Fisher PL, Durham RC. Recovery rates in generalized anxiety disorder following psychological therapy: An analysis of clinically significant change in the STAI-T across outcome studies since 1990. Psychol Med. 1999; 29: 1425–1434.
31. Den Oudsten BL, Zijlstra WP, De Vries J. The minimal clinical important difference in the World Health Organization Quality of Life instrument-100. Support Care. 2013; 21: 1295-1301.
32. Ware JE. SF-36 health survey: Manual and interpretation guide, 1993.
33. Hiroe T, Kojima M, Yamamoto I, et al. Gradations of clinical severity and sensitivity to change assessed with the Beck Depression Inventory-II in Japanese patients with depression. Psychiat Res. 2005; 135: 229–235.
34. Lin JM, Brimmer DJ, Maloney EM, Nyarko E, Belue R, Reeves WC. Further validation of the Multidimensional Fatigue Inventory in a US adult population sample. Popul Health Metrics. 2009; 7: 18.
35. Beck AT, Ward CH, Mendelson MM, Mock JJ, Erbaugh JJ. AN inventory for measuring depression. Arch Gen Psych. 1961; 4: 561–571.
36. The EuroQol Group. EuroQol - a new facility for the measurement of health-related quality of life. Health Pol. 1990; 16: 199–208.
37. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatrica Scandinavica. 1983; 67: 361–370.
38. Smets EMA, Garssen B, Bonke B, De Haes JCJM. The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res. 1995; 39: 315–325.
39. Zung WWK. A rating instrument for anxiety disorders. Psychosomatics. 1971; 12: 371–379.

40. Derogatis LR, Lipman RS, Covi L. SCL-90: An outpatient psychiatric rating scale- preliminary report. Psychopharmacol Bull. 1973; 9: 13–28.
41. Zung WK. A self-rating depression scale. Arch Gen Psych. 1965; 12: 63–70.
42. Sarason IG, Levine HM, Basham RB, Sarason BR. Assessing social support: The social support questionnaire. J Appl Soc Psychol. 1983; 44: 127–139.
43. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press, 1983.
44. Freyd M. The graphic rating scale. J Educ Psychol. 1923; 14: 83–102.
45. WHOQOL Group. Development of the WHOQOL: Rationale and current status. Int J Ment Health. 1994; 23: 24–56.
46. Lopes A, Frade IC, Teixeira L, Almeida M, Dias L, Henriques AC. Quality of life assessment in a living donor kidney transplantation program: Evaluation of recipients and donors. Transplant Proc. 2013; 45: 1106–1109.
47. Bergman S, Feldman LS, Mayo NE, et al. Measuring surgical recovery: The study of laparoscopic live donor nephrectomy. Am J Transplant. 2005; 5: 2489–2495.
48. Lumsdaine JA, Wray A, Power MJ, et al. Higher quality of life in living donor kidney transplantation: Prospective cohort study. Transpl Int. 2005; 18: 975–980.
49. Kok NFM, Lind MY, Hansson BME, et al. Comparison of laparoscopic and mini incision open donor nephrectomy: Single blind, randomised controlled clinical trial. British Med J. 2006; 333: 221–224.
50. Aguiar WF, Passerotti CC, Claro JFdA, et al. Mini-incisions by lombotomy or subcostal access in living kidney donors: A randomized trial comparing pain, safety, and quality of life. Clin Transplant. 2007; 21: 269–276.
51. Minnee RC, Bemelman WA, Polle SW, et al. Older living kidney donors: Surgical outcome and quality of life. Transplantation. 2008; 86: 251–256.
52. Bahler CD, Sundaram CP. Quality of life following laparoscopic living-donor nephrectomy. J Soc Laparoendoscopic Surgeons. 2013; 17: 273–278.
53. Klop KW, Kok NF, Dols LF, et al. Can right-sided hand-assisted retroperitoneoscopic donor nephrectomy be advocated above standard laparoscopic donor nephrectomy: A randomized pilot study. Transplant Int. 2013; 27: 162–169.
54. Smith GC, Trauer T, Kerr PG, Chadban SJ. Prospective psychosocial monitoring of living kidney donors using the SF-36 health survey. Transplantation. 2003; 76: 807–809.
55. Virzi A, Signorelli MS, Veroux M, et al. Depression and quality of life in living related renal transplantation. Transplant Proc. 2007; 39: 1791–1793.
56. Chien CH, Wang HH, Chiang YJ, Chu SH, Liu HE, Liu KL. Quality of life after laparoscopic donor nephrectomy. Transplant Proc. 2010; 42: 696–698.
57. Guleria S, Reddy VSK, Bora GS, Sagar R, Bhowmik D, Mahajan S. The quality of life of women volunteering as live-related kidney donors in India. Natl Med J India. 2011; 24: 342–344.
58. Vemuru Reddy SK, Guleria S, Okechukwu O, Sagar R, Bhowmik D, Mahajan S. Live related donors in India: Their quality of life using world health organization quality of life brief questionnaire. Indian J Urol. 2011; 27: 25–29.
59. Frade IC, Fonseca I, Dias L, et al. Impact assessment in living kidney donation: Psychosocial aspects in the donor. Transplant Proc. 2008; 40: 677–681.
60. Minz M, Udgiri N, Sharma A, et al. Prospective psychosocial evaluation of related kidney donors: Indian perspective. Transplant Proc. 2005; 37: 2001–2003.
61. Massey EK, Kranenburg LW, Zuidema WC, et al. Encouraging psychological outcomes after altruistic donation to a stranger. Am J Transplant. 2010; 10: 1445–1452.

62. Timmerman L, Zuidema WC, Erdman RAM, et al. Psychologic functioning of unspecified anonymous living kidney donors before and after donation. Transplantation. 2013; 95: 1369–1374.
63. Gross CR, Messersmith EE, Hong BA, et al. Health-related quality of life in kidney donors from the last five decades: Results from the RELIVE study. Am J Transplant. 2013; 13: 2924–2934.
64. Glotzer OS, Singh TP, Gallichio MH, Conti DJ, Siparsky NF. Longterm quality of life after living kidney donation. Transplant Proc. 2013; 45: 3225–3228.
65. Fukunishi I, Sugawara Y, Takayama T, Makuuchi M, Kawarasaki H, Surman OS. Association between pretransplant psychological assessments and posttransplant psychiatric disorders in livingrelated transplantation. Psychosomatics. 2002; 43: 49–54.
66. Rodrigue JR, Paek M, Whiting J, et al. Trajectories of perceived benefits in living kidney donors: Association with donor characteristics and recipient outcomes. Transplantation. 2014; 97: 762–768.
67. Schover LR, Streem SB, Boparai N, Duriak K, Novick AC. The psychosocial impact of donating a kidney: Long-term followup from a urology based center. J Urol. 1997; 157: 1596–1601.
68. Karrfelt HME, Berg UB, Lindblad FIE, Tyden GE. To be or not to be a living donor: Questionnaire to parents of children who have undergone renal transplantation. Transplantation. 1998; 65: 915–918.
69. Rodrigue JR, Cross NJ, Newman RC, et al. Patient-reported outcomes for open versus laparoscopic living donor nephrectomy. Prog Transplant. 2006; 16: 162–169.
70. Schwarz R, Krauss O, Hinz A. Fatigue in the general population. Onkologie. 2003; 26: 140–144.
71. Munch TN, Stromgren AS, Pedersen L, Petersen MA, Hoermann L, Groenvold M. Multidimensional measurement of fatigue in advanced cancer patients in palliative care: An application of the multidimensional fatigue inventory. J Pain Symptom Manag. 2006; 31: 533–541.
72. Kuhnt S, Ernst J, Singer S, et al. Fatigue in cancer survivors prevalence and correlates. Onkologie. 2009; 32: 312–317.
73. Yudkin PL, Stratton IM. How to deal with regression to the mean in intervention studies. Lancet. 1996; 347: 241–243.
74. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: What it is and how to deal with it. Int J Epidemiol. 2005; 34: 215–220.

Chapter 3

Consequences of living kidney donation: a prospective multicenter study

Wirken L, van Middendorp H, Hooghof CW, Sanders JSF, Dam RE, van der Pant KAMI, Wierdsma JM, Wellink H, van Duijnhoven EM, Hoitsma AJ, Hilbrands LB, Evers AWM

In revision.

ABSTRACT

Previous studies indicated a decrease of health-related quality of life (HRQoL) shortly after kidney donation, returning to baseline on the longer-term. However, a subgroup experiences persistent HRQoL problems. The current study examined the HRQoL course up to 12 months post-donation and donor-perceived consequences of the donation for donors, recipients, and donor-recipient relationships. This prospective study was conducted in seven Dutch transplantation centers, with 230 donors completing self-report questionnaires before and 6 and 12 months post-donation. Results indicated that donor physical HRQoL was comparable at all time points, except for an increase in fatigue that lasted up to 12 months post-donation. Mental HRQoL was decreased at 6 months post-donation, but returned to baseline at 12 months. Donors reported large improvements in recipient functioning and a smaller influence of the recipient's kidney disease or transplantation on the donor's life over time. Physical, emotional, and relational consequences of donation were limited. A small donor subgroup does experience negative donation consequences (e.g., regret). Looking more closely into regret, donation type and donor-recipient relationship did not differ between donors with and without regret, whereas more negative health perceptions and worse social functioning six months after donation significantly predicted regret at twelve months after donation. Future research should examine predictors of donor's HRQoL after donation, to improve screening, and to provide potential interventions in those at-risk donors.

INTRODUCTION

Prospective studies in living kidney donors have shown small decreases in health-related quality of life (HRQoL) shortly after donation, generally returning to baseline on the longer-term (1-3). However, uncertainty (e.g., regarding recipient outcome) and distress about the screening or surgery (4, 5) may lead to more serious HRQoL-problems in some donors, such as anxiety or fatigue (1, 6, 7). To identify which HRQoL-aspects are impacted most by the donation and identify at-risk (potential) donors, more specific insight into the consequences of donation is needed.

Previous research on HRQoL in living kidney donors has mostly used generic HRQoL-instruments that do not capture specific relevant donation-related domains (8, 9). Furthermore, the donor's perception on donation consequences for themselves, the recipient, and their relationship before and after transplantation were mostly described in retrospective or qualitative studies (10-14). Also, the presence or absence of regret about the donation decision was mostly assessed using a single ad hoc question indicating that a small subgroup of donors experiences regret (11, 15-17). Previous research assessing decisional regret about healthcare decisions in other patient populations showed that more regret was related to poorer HRQoL. Adverse health outcomes, more ambivalence, and lower satisfaction about information provision are potential predictors of regret (18, 19). Whether such variables also predict regret in kidney donors has not been studied.

The current study aims to improve our insight into the potential consequences of living kidney donation by prospectively examining the course of generic HRQoL as well as donation-specific domains.

MATERIALS AND METHODS

Procedure

During the data collection period (2011-2015) all donor candidates from seven Dutch transplantation centers (Radboud university medical center, University Medical Center Utrecht, Leiden University Medical Center, University Medical Center Groningen, Maastricht University Medical Center, Academic Medical Center Amsterdam, and VU University Medical Center Amsterdam) were invited to participate in the study after their first screening visit. Illiteracy was the only exclusion criterion. After signing informed consent, a questionnaire was sent either by email or on paper. Donors received a similar questionnaire six and twelve months after surgery. The Ethics Committee of the Radboud university medical center decided that the study did not fall within the scope of the Medical Research Involving Human Subjects Act. Moreover, since the study did not

pose any risk for participants, approval by an ethics committee was not required. In all participating centers, the executive board approved the study. The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul and the Declaration of Helsinki.

Participants

A total of 588 donor candidates filled out the questionnaire after the first screening visit (75% response rate), of whom 361 donors (61%) donated their kidney. The mean time between screening and donation was 7.0±5.2 months. Reasons for exclusion from the donation procedure are presented in Figure 1. Complete data of 230 donors were available.

Measures

1) Pre-donation demographic, intra- and postoperative characteristics

Demographic and intra- and post-operative factors were assessed (e.g., surgery type, hospital stay, complications). Donor complications were derived from the donor's medical files and defined using the Dindo-Clavien classification system (20). Data on recipient's pre-transplantation treatment and post-transplantation outcome (i.e., graft failure or death) were derived from the Dutch Organ Transplantation Registration system (21).

2) Health-related quality of life (HRQoL)

Physical functioning before, and 6 and 12 months post-donation, was assessed using the RAND Short Form-36 Health Status Inventory (RAND-SF36; 22) and Checklist Individual Strength-Fatigue Short Version (CIS; 23).

The RAND-SF36 is a 36-item questionnaire assessing eight HRQoL-dimensions. Physical HRQoL consists of the subscales Physical Functioning, Role Limitations due to Physical Health Problems, Pain, and General Health Perceptions, summarized in the Physical Health Composite Score. The Hays norm-based scoring algorithm was applied, transforming raw scores into T-scores (M=50±10 in the general population) (22). Higher scores represent better HRQoL. Cronbach's alphas varied between .53 (General Health Perceptions) and .91 (Role limitations due to Physical Health Problems).

The CIS short version (23) (4 items) assesses fatigue (e.g., 'I feel tired'). Higher scores represent more fatigue. Cronbach's alpha was .80.

Psychological functioning before, and 6 and 12 months post-donation was assessed using the RAND-SF36 mental HRQoL scales Emotional Well-being, Role Limitations due to Emotional Problems, Social Functioning, and Energy, summarized in the Mental Health Composite Score (22). Cronbach's alphas varied between .61 (Social Functioning) and .83 (Mental Health Composite).

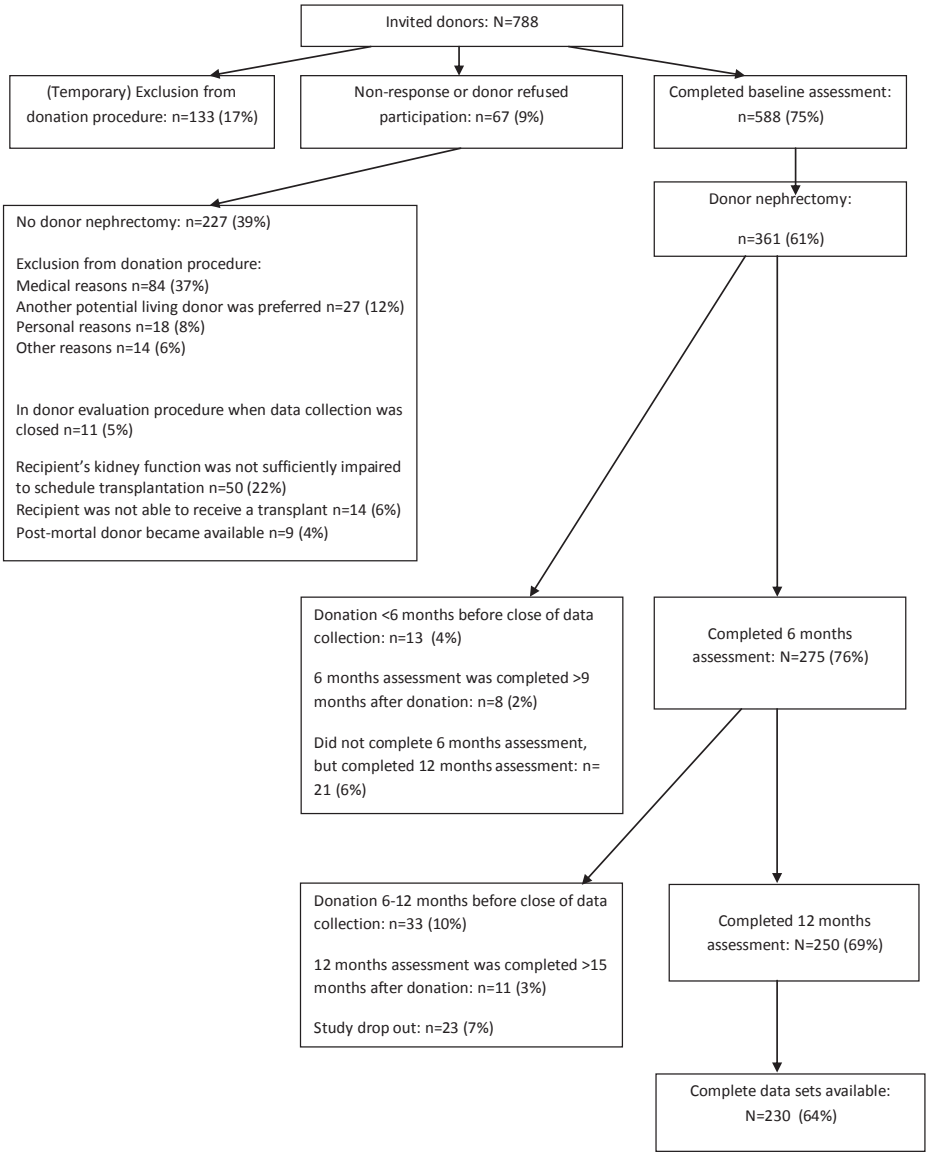


Figure 1. Study Flow Chart

3) Donor-perceived and recipient-related consequences of donation

Course of donor and recipient-related functioning

The impact of (intended) donation on the donor, recipient, or donor-recipient relationship was assessed before, and 6 and 12 months post-donation using Visual Analogue Scales (VAS; Supplement 1). The domains assessed were donor perspectives on 1) current recipient's physical and emotional functioning, 2) recipient limitations caused by

the kidney disease or transplantation, 3) quality of the donor-recipient relationship, 4) influence of recipient's kidney disease on the donor's daily life, 5) donor responsibility for recipient's wellbeing, and 6) the extent to which the donor takes care of tasks that the recipient cannot accomplish due to the kidney disease/transplantation. Altruistic donors did not complete these questionnaires. Donors within a kidney exchange program were asked to think about their known recipient when completing the questionnaires.

Perceived donation consequences

We developed a new questionnaire to specifically assess donor perceived consequences of donation and transplantation for the donor, recipient, and their relationship (Supplement 2). Relevant items were based on evaluation of scientific literature and on clinical practice. The questionnaire was first evaluated by a small group of donors to test usability. After revision, Principal Component Exploratory Factor Analysis with Promax rotation and Kaiser Normalization was used to identify the scale structure. This Perceived Donation Consequences Scale (PDCS) consisted of 29 items measured on a 5-point Likert scale (1=strongly disagree, 5=strongly agree) and showed a consistent four-factor structure in the six and twelve months post-donation assessments. The factors assessed donor physical consequences (5 items; e.g., 'My recovery from surgery took longer than I expected.'), post-donation worries (5 items; e.g., 'I am concerned about the performance of my remaining kidney in the future.'), recipient consequences (3 items; e.g., 'The disease burden of the recipient in daily life has been reduced.'), and relational consequences (5 items; e.g., 'I expected more appreciation and attention from the recipient.'). Higher scores represent a greater impact of donation. Eleven items were excluded because of factor loadings ≤.40 or cross-loadings ≥.20, leaving a total number of 18 items. Cronbach's alphas varied between .65 (post-donation worries) and .86 (recipient and relational consequences).

Regret about the donation decision was assessed 12 months post-donation using the Decision Regret Scale, measuring distress or remorse about healthcare decisions (19). In this 5-item questionnaire (e.g., 'It was the right decision.'), scores were converted to 0-100 scales. Higher scores indicate a higher degree of regret. Cronbach's alpha was .86. The percentage of donors experiencing decisional regret was expressed by using a cut-off score≥30 (18).

Statistical analyses

Normal distribution was verified, transforming skewed or kurtosed variables using logarithmic or reflected transformations in order to enable parametric statistics. Generalized mixed-model analyses were conducted to examine the HRQoL course from before to 6 and 12 months post-donation on 1) RAND-SF36 Physical and Mental Health Composite Scores and CIS fatigue, and 2) RAND-SF36 subscales. HRQoL scores were also compared

with population norms. Clinically relevant differences between time points were defined as 5-point differences in T-scores using the RAND-SF36 (22) and 0.5 SD differences of norm scores using the CIS (23).

Changes in perceived donor and recipient functioning and donor-recipient interaction (0-10 VAS-scales) were assessed by means of generalized mixed models. In addition, VAS-scores were categorized into 4 classes: poor (score 0-0.4), fair (0.5-4.4), moderate (4.5-7.4), and good functioning (7.5-10.0) (24). Similarly, for each factor of the PDCS, mean scores for donation consequences on 5-point Likert-scales were categorized into 3 classes: no-few consequences (*M*=1.0-1.9), some consequences (*M*=2.0-3.9), and many consequences (*M*=4.0-5.0). Pearson correlation analyses were conducted to examine the association of donor demographic characteristics, pre-, intra- and post-operative donor and recipient health status, and donor measures with regret about the donation decision at 12 months post-donation. Subsequently, to examine the relative contribution of potential predictors, all variables that showed significant correlations to regret at twelve months post-donation were included in hierarchical multiple regression analyses. Analyses were conducted using IBM SPSS Statistics 22.0 (25).

RESULTS

Donor characteristics

Table 1 presents demographic, intra-operative and postoperative characteristics of 230 participating donors. The sexes were almost equally represented (59% female), mean age was 55.1 (SD=10.7; range 23-76) years, and most participants had secondary level education (62%). The majority (83%) donated directly to a recipient they knew and underwent laparoscopic surgery (85%). Most donors did not experience complications (83%) and in a minority of recipients there was graft failure (6%) or death (3%) within the first year after transplantation. Mean post-donation hospital stay was 4.6 (SD=1.6; range 1-14) days.

Table 1. Demographic characteristics and donor and recipient intra-operative and postoperative factors

Characteristic	Mean ± sd (range) N (%)
Baseline demographic characteristics	
Age (years)	55.1 ±10.7 (23-76)
Gender	
Female	59%
Male	41%
Marital status[a]	
Single	19%
Steady partner	81%
Educational level[b]	
Primary education	5%
Secondary education	62%
Tertiary education	33%
Donation type	
Direct	83%
Kidney exchange procedure	8%
Anonymous	9%
Donor-recipient relationship	
Spouse	30%
Parent	20%
Sibling	18%
Child	3%
Other - related	17%
Other - unrelated	3%
Anonymous	9%
Religious affiliation[b]	
Religious	53%
Non-religious	47%
Ethnicity	
Dutch	95%
Other	5%
Donor intra-operative and postoperative characteristics	
Surgery type	
Mini-incision donor nephrectomy	15%
Laparoscopy	85%
Hospital stay (days)	4.6 ± 1.6 (1-14)
Donor complications[c]	
No complications	83%
Grade I	9%
Grade II	7%
Grade III a	0%

Table 1. Demographic characteristics and donor and recipient intra-operative and postoperative factors (continued)

Characteristic	Mean ± sd (range) N (%)
Grade III b	1%
Grade IV a	0%
Grade IV b	0%
Grade V	0%
Recipient complications	
Graft failure	
No	94%
Yes	6%
Patient death	
No	97%
Yes	3%

[a] n=228 [b] n=229

[c] Categorisation according the Clavien-Dindo classification system; Grade I: no need for therapeutic interventions; Grade II: pharmacological treatment required, Grade III: surgical, endoscopic, or radiological intervention required (a) not under general anaesthesia or b) under general anaesthesia); Grade IV: Life-threatening complication requiring IC/ICU management for (a) single organ dysfunction or b) multi-organ dysfunction); and Grade V: patient death (Dindo et al. 2004).

1) The HRQoL course

Mean physical and mental HRQoL scores pre- and post-donation are reported in Table 2.

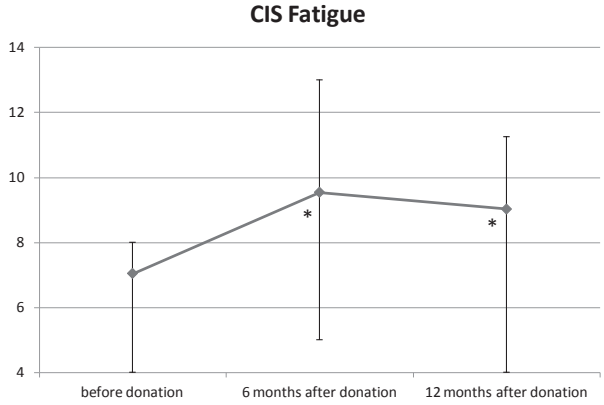


Figure 2. The course (means and interquartile range) of CIS Fatigue before, and six and twelve months after donation

*significant at $p<.05$ level in comparison to baseline level

Table 2. Descriptive statistics (Mean ± sd) of donor self-report measures of HRQoL and fatigue

	Before donation	6 months after donation	pre-donation vs. 6 months after donation	12 months after donation	pre-donation vs. 12 months after donation	6 months vs. 12 months after donation
	Mean ± sd (range)	Mean ± sd (range)	*p*	Mean ± sd (range)	*p*	*p*
Health-related quality of life						
Physical HRQoL (RAND SF36)						
Physical Health Composite Score*	55.6 ± 4.5 (34.0-61.0)	54.9 ± 7.0 (22.0-61.0)	.55	55.5 ± 6.6 (22.0-61.0)	.06	.06
Physical functioning*	55.7 ± 3.9 (27.0-58.0)	54.1 ± 5.7 (26.0-58.0)	<.001	54.9 ± 5.7 (24.0-58.0)	.20	.001
Role limitations - physical health problems*	55.0 ± 4.9 (26.0-56.0)	51.9 ± 9.0 (26.0-56.0)	<.001	53.0 ± 7.8 (26.0-56.0)	<.001	.049
Pain*	56.9 ± 6.0 (25.0-60.0)	57.3 ± 6.4 (22.0-60.0)	.26	57.4 ± 6.5 (22.0-60.0)	.09	.35
General health perceptions	53.3 ± 6.9 (36.0-64.0)	55.1 ± 7.3 (32.0-64.0)	.001	55.0 ± 7.7 (29.0-64.0)	.002	.85
Fatigue (CIS short version)						
Fatigue*	7.0 ± 3.8 (4.0-26.0)	9.5 ± 6.1 (4.0-28.0)	<.001	9.0 ± 6.0 (4.0-28.0)	<.001	.10
Psychological HRQoL (RAND SF36)						
Mental Health Composite Score*	55.2 ± 6.5 (31.0-66.0)	53.4 ± 8.6 (25.0-66.0)	.01	54.6 ± 8.5 (22.0-66.0)	.66	<.001
Emotional wellbeing	53.1 ± 7.5 (28.0-66.0)	52.5 ± 8.8 (29.0-66.0)	.25	53.6 ± 8.4 (27.0-66.0)	.36	.03
Role limitations - mental health problems*	52.7 ± 5.2 (19.0-54.0)	51.4 ± 7.9 (19.0-54.0)	.02	51.6 ± 8.0 (19.0-54.0)	.07	.69
Energy	56.8 ± 7.4 (35.0-70.0)	54.2 ± 8.8 (30.0-70.0)	<.001	55.7 ± 8.8 (30.0-70.0)	.07	.001
Social functioning*	54.3 ± 5.5 (31.0-57.0)	52.4 ± 7.9 (17.0-57.0)	.002	52.9 ± 7.5 (20.0-57.0)	.01	.40

RAND SF36: RAND Short Form-36 Health Status Inventory; CIS: Checklist Individual Strength

*variable transformed in analyses because of no normal distribution

Physical functioning

Physical HRQoL (RAND-SF36 PCS) did not significantly change from before to twelve months post-donation. Median scores were within 1 SD above population norms at all time points.

Fatigue scores changed significantly over time, with higher fatigue levels at six (p<.001) and twelve (p<.001) months post-donation as compared to pre-donation, and comparable levels of fatigue at both post-donation assessments (Figure 2). Pre-donation fatigue scores were comparable to general population norms, but post-donation fatigue scores were 0.5 SD higher.

Regarding the specific aspects of physical HRQoL (RAND-SF36 subscales), physical functioning changed significantly over time (Figure 3), with a decrease of functioning from before to six months post-donation (p<.001), and an increase to baseline from 6 to 12 months post-donation (p=.001). Also, role limitations due to physical health problems changed significantly over time, with an increase of role limitations from before to six months post-donation (p<.001), which decreased from six to twelve months post-donation (p=.049) up to a level above baseline (p<.001). Furthermore, significant changes in general health perceptions were indicated, with worse general health perceptions pre-donation than at six (p=.001) and twelve months (p=.002) post-donation. No difference between both post-donation assessments was found. Pain did not significantly change over time.

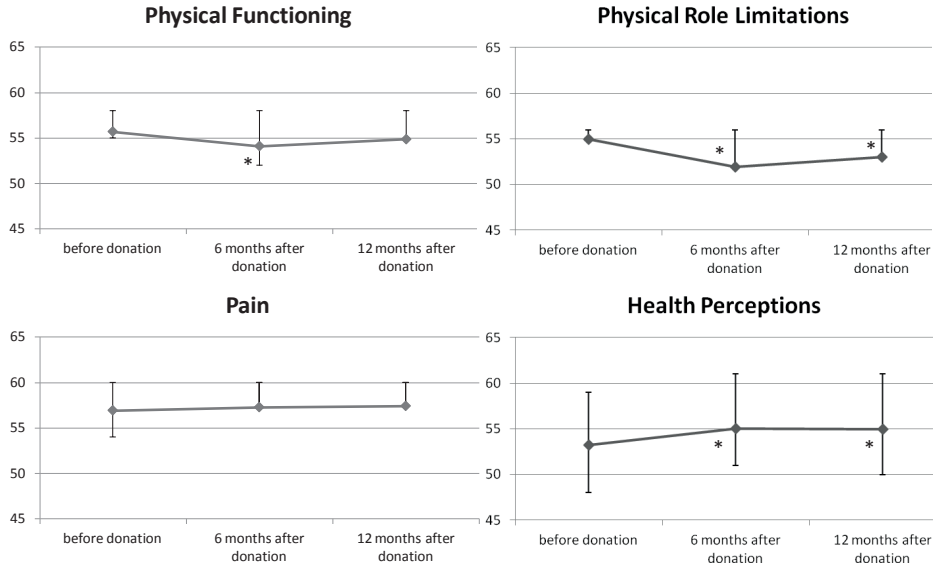


Figure 3a-d: The course (means and interquartile range) of physical HRQoL subscales (RAND-SF36) before, and six and twelve months after donation

*significant at p<.05 level in comparison to baseline level

Psychological functioning

Mental HRQoL (RAND-SF36 MCS) changed significantly over time (p=.001), with a decrease of functioning from before to six months post-donation (p=.01), and an increase to baseline from 6 to 12 months post-donation (p=.001). Median scores were within 1 SD above population norms at all time points.

Concerning the specific aspects of mental HRQoL (Figure 4), no overall time effects were found for emotional wellbeing and role limitations due to mental health problems. Energy levels changed significantly over time (p<.001), with higher energy levels before donation than six months post-donation (p<.001), which significantly increased from six to twelve months post-donation (p=.001) but remained marginally lower than before donation at twelve months post-donation (p=.07). Last, social functioning changed significantly over time (p=.01), with better functioning pre-donation than six (p=.002) and twelve (p=.01) months post-donation, with no significant difference between both post-donation assessments.

Clinically relevant HRQoL changes between the three assessment points were only found for fatigue. No differences on the outcomes were found between donors who completed all three assessments and donors who dropped out of the study.

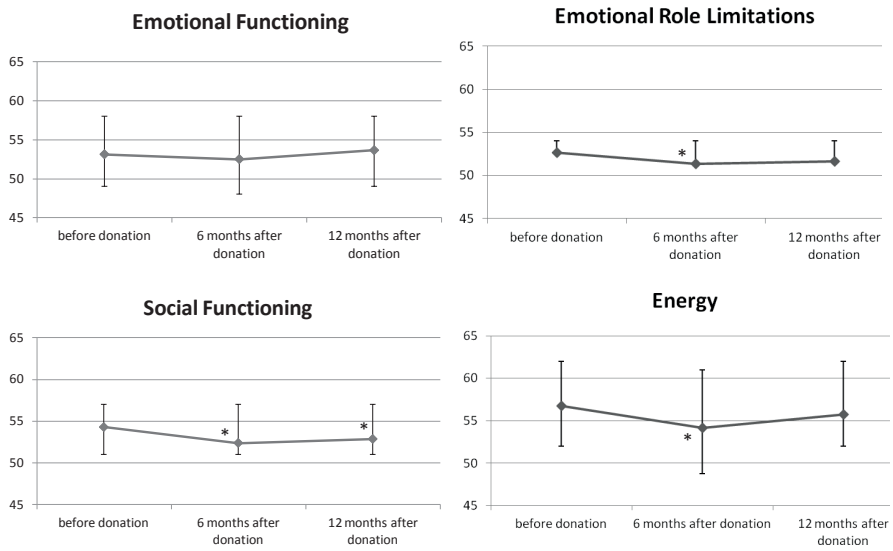


Figure 4a-d: The course (means and interquartile range) of mental HRQoL subscales (RAND-SF36) before, and six and twelve months after donation

*significant at p<.05 level in comparison to baseline level

Table 3. Descriptive statistics (Means ± sd) of donor perceived donor- and recipient-related functioning.

	Before donation		6 months after donation		pre-donation vs. 6 months after donation	12 months after donation		pre-donation vs. 12 months after donation	6 months vs. 12 months after donation
	Means ± sd (range)	%	Means ± sd (range)	%	*p*	Means ± sd (range)	%	*p*	*p*
Donor perceived donor- and recipient-related functioning (VAS-scales 0-10)									
Physical functioning of the recipient[1]	4.8 ± 2.0 (0.4-10.0)		7.6 ± 1.9 (0.0-10.0)		<.001	7.7 ± 1.8 (0.0-10.0)		<.001	.88
poor (0.0-0.4)		1%		2%			1%		
fair (0.5-4.4)		44%		4%			4%		
moderate (4.5-7.4)		45%		32%			27%		
good (7.5-10.0)		10%		62%			68%		
Emotional wellbeing of the recipient[1]	6.6 ± 1.7 (1.5-10.0)		7.9 ± 1.7 (0.0-10.0)		<.001	7.9 ± 1.9 (0.0-10.0)		<.001	.81
poor (0.0-0.4)		0%		2%			1%		
fair (0.5-4.4)		13%		1%			4%		
moderate (4.5-7.4)		51%		27%			21%		
good (7.5-10.0)		36%		70%			74%		
Limitations for the recipient caused by the kidney disease or transplantation[1]	4.4 ± 2.2 (0.0-10.0)		6.9 ± 2.1 (0.0-10.0)		<.001	7.4 ± 1.9 (0.0-10.0)		<.001	.04
many (0.0-0.4)		2%		2%			1%		
some (0.5-4.4)		52%		10%			7%		
few (4.5-7.4)		36%		37%			31%		
no (7.5-10.0)		10%		51%			61%		
Quality of the donor-recipient relationship[1*]	8.7 ± 1.1 (3.0-10.0)		8.5 ± 2.0 (0.0-10.0)		.24	8.7 ± 1.6 (0.0-10.0)		.97	.27
poor (0.0-0.4)		0%		3%			1%		
fair (0.5-4.4)		1%		2%			1%		
moderate (4.5-7.4)		7%		9%			8%		
good (7.5-10.0)		92%		86%			90%		

Table 3. Descriptive statistics (Means ± sd) of donor perceived donor- and recipient-related functioning. (continued)

	Before donation		6 months after donation		pre-donation vs. 6 months after donation	12 months after donation		pre-donation vs. 12 months after donation	6 months vs. 12 months after donation
	Means ± sd (range)	%	Means ± sd (range)	%	*p*	Means ± sd (range)	%	*p*	*p*
Influence of the recipient's kidney disease on the life of the donor[2]	4.9 ± 2.8 (0.0-10.0)		3.2 ± 3.0 (0.0-10.0)		<.001	2.9 ± 3.0 (0.0-10.0)		<.001	.04
no (0.0-0.4)		8%		16%			18%		
little (0.5-4.4)		33%		51%			53%		
moderate (4.5-7.4)		37%		17%			15%		
much (7.5-10.0)		22%		16%			14%		
Donor feelings of responsibility for the wellbeing of the recipient[2]	5.6 ± 3.1 (0.0-10.0)		4.1 ± 3.2 (0.0-10.0)		<.001	4.3 ± 3.5 (0.0-10.0)		<.001	.85
no (0.0-0.4)		9%		11%			15%		
few (0.5-4.4)		23%		42%			34%		
some (4.5-7.4)		33%		23%			24%		
many (7.5-10.0)		35%		24%			27%		
Donor taking care of recipient tasks which cannot be accomplished due to the kidney disease[2]	2.6 ± 3.0 (0.0-10.0)		1.6 ± 2.4 (0.0-10.0)		<.001	1.4 ± 2.1 (0.0-9.0)		<.001	.32
no (0.0-0.4)		36%		34%			40%		
little (0.5-4.4)		36%		50%			48%		
moderate (4.5-7.4)		18%		10%			8%		
many (7.5-10.0)		10%		6%			4%		

[1]higher scores represent higher wellbeing [2]higher scores represent lower wellbeing .

*variable transformed in analyses because of no normal distribution

Donor-perceived consequences of donation

The course of donor- and recipient-related functioning

The quality of the donor-recipient relationship did not change over time and was perceived very positively (86-92%). Donors reported that the physical and emotional functioning of their recipients markedly improved over time ($p<.001$). Recipient's physical functioning was perceived as good (VAS≥7.5) by only 10% of donors pre-donation, and by 62-68% six and twelve months post-donation. Recipient's emotional wellbeing was perceived as good by only 36% of donors pre-donation, and by 70-74% six and twelve months after donation. Furthermore, donors perceived fewer recipient limitations in daily life at both six and twelve ($p<.001$) months after transplantation. Also, after transplantation, the donor's life was less influenced by the recipient's kidney disease ($p<.001$), with 59% of donors experiencing moderate-much influence pre-donation, and 29-33% six and twelve months post-donation. Lastly, donors felt less responsible for recipient's wellbeing ($p<.001$) and donors took over fewer recipient's tasks than before transplantation ($p<.001$) (Table 3).

Perceived donation consequences (PDCS)

The scores on post-donation negative physical or relational consequences were low. Only 5% of donors had a score of 4 or more (on a five-point scale) on negative physical consequences, and for negative relational consequences this percentage was even lower (1%). The majority of donors reported positive recipient outcomes at six (80%) and twelve (82%) months after transplantation. Nevertheless, many (57-66%) donors reported some degree of post-donation worries (Table 4). Changes in donor perceived consequences of donation over time were only found for physical consequences, which were perceived to a lesser extent at twelve than six months after donation ($p=.003$) (Table 4).

Regret towards the donation decision

One year post-donation, most donors had no to minimal feelings of regret about the donation decision (Median=5.0, IQR 0-20, on a 0-100 scale). Fourteen percent of the donors reported substantial feelings of regret. Higher levels of regret were associated with different pre-donation factors, namely worse emotional functioning of the recipient ($r=-.15$), more donor feelings of responsibility about the recipient ($r=.15$), higher expectations about donor benefits ($r=.16$), more anxiety ($r=.17$), and lower age ($r=-.14$). Also, more influence of the recipient's transplantation on the donor's life ($r=.18$), worse health perceptions ($r=-.15$), worse social functioning ($r=-.14$), and worse surgery recovery ($r=-.37$) six months post-donation were related to more regret twelve months post-donation. No significant relationships between regret and different donation types or donor-recipient relationships were found. From multiple regression analyses, worse

Table 4. Descriptive statistics (Means ± sd) of donor perceived donation consequences and regret.

Perceived donation consequences *(Perceived Donation Consequences Scale)*[3]	**6 months after donation**		**12 months after donation**		**6 vs. 12 months post-donation**
	Means ± sd (range)	**%**	**Means ± sd (range)**	**%**	***p***
Negative physical consequences	2.1 ± 0.9		2.0 ± 0.9		.003
In retrospect the surgery was worse than anticipated.	(1.0-4.8)	No/few 47%	(1.0-5.0)	No/few 57%	
I still frequently experience physical symptoms like pain and fatigue due to the donation.		Some 48%		Some 39%	
My recovery from surgery took longer than I expected.		Many 5%		Many 4%	
I have not been able to resume all my day-to-day routines.					
The physical effects of the donation were greater than I expected.					
Post-donation worries	2.1 ± 0.7		2.1 ± 0.7		.28
I found it difficult to get used to the idea that I only have one kidney.	(1.0-3.8)	No/few 34%	(1.0-4.2)	No/few 42%	
I still find myself quite preoccupied by the donation.		Some 66%		Some 57%	
I am concerned about the performance of my remaining kidney in the future.		Many 0%		Many 1%	
I am concerned about how the kidney I donated will function in the future.					
I'm finding it difficult to let go of my care for the recipient after the donation.					
Positive recipient consequences	4.2 ± 0.8		4.3 ± 0.7		.64
The quality of life of the recipient has improved due to the donation.	(1.0-5.0)	No/few 2%	(1.0-5.0)	No/few 2%	
The disease burden of the recipient in daily life has been reduced.		Some 18%		Some 16%	
The risks for the recipient as a consequence of the kidney disease have been reduced due to the donation.		Many 80%		Many 82%	
Negative relational consequences	1.5 ± 0.6		1.5 ± 0.6		.72
Relations within the family/ with my partner have changed for the worse since the donation.	(1.0-4.4)	No/few 79%	(1.0-5.0)	No/few 78%	
My relationship with the recipient has changed for the worse due to the donation.		Some 20%		Some 21%	
The relationship with the recipient has been put under pressure.		Many 1%		Many 1%	
I expected more appreciation and attention from the recipient.					
My relationships with relatives of the recipient have changed for the worse due to the donation.					
Regret about the donation decision (Decision Regret Scale)[4]					
Decisional Regret			12.2 ± 21.8		
No feelings of regret (<30)			(0-100)	86%	
Substantial feelings of regret (≥30)				14%	

[3]higher scores represent more donor consequences [4]higher scores represent more decisional regret

health perceptions (β=-.21, *p*=.022) and worse social functioning (β=-.23, *p*=.035) six months post-donation were significant predictors of more regret twelve months post-donation, while no significant predictors on baseline were found.

DISCUSSION

The current study examined the course of HRQoL and donor- and recipient-related donation consequences from the donor's perspective. Donor physical and mental HRQoL was largely comparable at all time points. There was a temporary decrease for some aspects of physical and psychological functioning at 6 months post-donation, but most levels had returned to baseline at 12 months post-donation. Also, scores were above population norms at all time points. Persistent and clinically relevant changes were only found for fatigue, which increased post-donation up to one year. The donors reported a low rate of negative donation consequences concerning themselves, the recipients, or their relationship with the recipient, and reported low levels of regret. Instead, they perceived a strong improvement in recipient's functioning and a reduced influence of the kidney disease on their own life.

The stability of physical functioning over time indicates that most donors are physically recovered from surgery during the first months post-donation, as was found in previous studies (2, 26). However, complaints of fatigue persisted on the longer-term, indicating that fatigue is the aspect of physical functioning that is mostly affected by donation, which is in line with the conclusion from our meta-analysis on HRQoL consequences of kidney donation (2). Potential causes of these elevated fatigue levels are currently unknown, with physical (surgery consequences), but also behavioral or cognitive possible causes (donation or recipient worries, or regret) (27).

The temporary decrease of mental HRQoL six months post-donation might be the consequence of the resumption of daily life activities after surgery, which could lead to a higher physical and mental burden. Further, donors mostly received a lot of attention during the donation procedure, both from the hospital and relatives. However, afterwards, attention for donors diminishes or shifts back to the recipient, and everything is expected to be back to normal (13, 28). Therefore, opportunities of sharing donation experiences or potential worries and feelings of social support could decrease, which could potentially lead to a poorer mental HRQoL.

Whereas most previous studies have focused primarily on the course of generic HRQoL after kidney donation, the current study included a broad range of donation-specific consequences, including donor-perceived consequences for both donor and recipient and their relationship, post-donation worries, and regret. In line with previous studies, donation experiences were mainly positive, with small percentages of donors (0-5%) re-

porting negative physical and relational consequences and post-donation worries. The percentage of donors experiencing a substantial level of regret one year post-donation found in the current study (14%) is higher than the levels which were found in previous studies. However, it is comparable to percentages reported in a systematic review on decision regret with regard to different kinds of healthcare decisions. Potentially, the use of a quantitative multidimensional measurement of regret (The Decision Regret Scale) could provide other information about the extent to which donors experience regret. More regret was associated with different demographic, HRQoL, and recipient-related factors, but not with donation type or donor-recipient relationship. Because no pre-donation predictors but only more negative health perceptions and worse social functioning six months after donation predicted longer-term regret, post-donation monitoring seems indicated to provide interventions to high-risk donors to prevent the onset or deterioration of regret after donation. Furthermore, as was found that regret could change over time (18), it would be relevant to examine whether donor regret persists or abates on the long-term.

Donors reported improvements of recipient's physical and emotional functioning after transplantation, which reflect a desired donation outcome, which is often a major motivation to donate. This improvement of recipient's HRQoL was also, and perhaps more objectively, confirmed by the decreased influence of the recipient's kidney disease on the donor's life. Although the increase of recipient's HRQoL after kidney transplantation is known from previous studies (29, 30), the donor perspective hereon was not prospectively studied before. Also, the influence of recipient's kidney disease on the donor's life, both before and after donation is a relatively new theme in transplantation literature, because most studies specifically focus on the influence of recipient graft failure or death.

A small proportion of donors experienced negative donation consequences (decreased HRQoL, adverse effects on the donor-recipient relationship, or regret). Future research should identify risk factors of donor's HRQoL after donation and develop interventions for (potential) donors at risk. Furthermore, in order to prevent unrealistic expectations, consultations of healthcare professionals with potential donors should focus on evidence-based information regarding the potential consequences of kidney donation, discussion of alternative treatment options, expectations of the transplantation for the recipient, and on the preferences and values of the potential donor.

This multi-center study in a large and representative population of kidney donors gives insight into the course of HRQoL from before to 12 months post-donation, and evaluates donor-perceived consequences of donation with regard to their own, recipient, and mutual functioning. Ideally, a study like this one should include a relevant control group. However, a comparable control group of eligible donors who eventually do not donate was not available. Instead, HRQoL results were compared with population norms and

clinically relevant differences between time points were assessed to frame results. The group of donors whose recipient experienced graft failure or death was very small (3-6%), which is a very good outcome, but complicates the reliable assessment of the influence of recipient complications on donors' HRQoL course. Future research should examine long-term consequences of donation. Most donors included had the Dutch nationality. Also, the healthcare setting of kidney donors in the Netherlands, in terms of access to care and regulations for health insurance, is well-organized and available to all inhabitants. Therefore, the generalization of findings has to be studied.

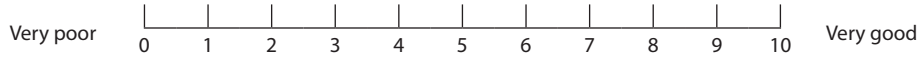
In conclusion, for most donors, the donation procedure has few negative consequences. Concerning HRQoL changes, small temporary decreases returned to baseline within one year post-donation and scores remained at or above population norms. The clinically relevant and persistent impact of donation on fatigue, which has been previously reported, warrants specific attention. That a small subgroup of donors was found to experience negative HRQoL consequences, underlines the relevance for further research into predictors of these outcomes, which would enable improved screening and potential interventions in those at-risk donors.

Supplement 1. Consequences of living kidney donation: a prospective multicenter study

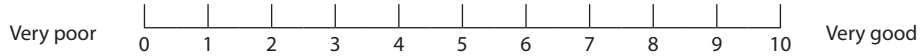
The questions below are about how you, as a donor, rate the wellbeing of the recipient. Please rate the wellbeing of the recipient by placing a checkmark on the scale. The better the wellbeing of the recipient, the further to the right the checkmark is placed.

(Remark: In kidney exchange programs, your kidney was donated to an unknown person. When the questions below refer to 'the recipient', please rate for your own recipient.)

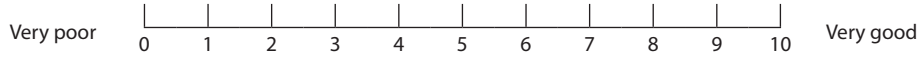
1. How do you rate the relationship with the recipient at the present time?



2. How do you rate the physical functioning of the recipient at the present time?



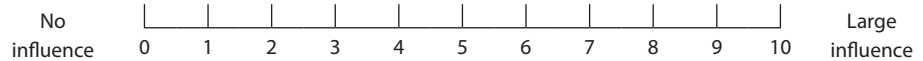
3. How do you rate the emotional wellbeing of the recipient at the present time?



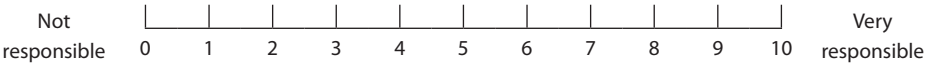
4. In your opinion, how many limitations does the recipient currently experience in day-to-day life due to the kidney disease or the transplantation?

The questions below concern the impact that the recipient's kidney disease or transplantation has on your own life at the present time:

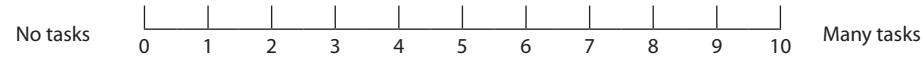
5. To what extent is your life currently influenced by the recipient's kidney disease or transplantation?



6. To what extent do you currently feel responsible for the wellbeing of the recipient?



7. Do you currently take over tasks from the recipient, which he or she cannot accomplish due to the kidney disease or transplantation?



Supplement 2. Perceived Donation Consequences Scale

Below you find a number of statements about the donation. Please indicate for each statement to what extent it applies to your situation.

		Totally disagree	*Disagree*	*Don't agree/ Don't disagree*	*Agree*	*Totally agree*
1.	My own quality of life has improved due to the donation.	1	2	3	4	5
2.	The response of my spouse and/or children has not been as positive as I had expected.	1	2	3	4	5
3.	The response of relatives to the donation has not been as positive as I had expected.	1	2	3	4	5
4.	If I had to make the choice again, I would certainly choose to donate a kidney.	1	2	3	4	5
5.	In retrospect the surgery was worse than anticipated.	1	2	3	4	5
6.	I still frequently experience physical symptoms like pain and fatigue due to the donation.	1	2	3	4	5
7.	My expectations before the donation were realistic.	1	2	3	4	5
8.	Relations within the family/ with my partner have changed for the worse since the donation.	1	2	3	4	5
9.	I would always recommend others to donate a kidney.	1	2	3	4	5
10.	I found it difficult to get used to the idea that I only have one kidney.	1	2	3	4	5
11.	My recovery from surgery took longer than I expected.	1	2	3	4	5
12.	The relationships with family and friends have improved due to the donation.	1	2	3	4	5
13.	I have not been able to resume all my day-to-day routines.	1	2	3	4	5
14.	I still find myself quite preoccupied by the donation.	1	2	3	4	5
15.	The physical effects of the donation were greater than I expected.	1	2	3	4	5
16.	The concerns I had before the donation proved unfounded.	1	2	3	4	5

		Totally disagree	*Disagree*	*Don't agree/ Don't disagree*	*Agree*	*Totally agree*
17.	I am concerned about the performance of my remaining kidney in the future.	1	2	3	4	5
18.	My faith or personal beliefs have been strengthened though the donation.	1	2	3	4	5
19.	I am concerned about how the kidney I donated will function in the future.	1	2	3	4	5

The questions below concern the recipient of your kidney.

In **kidney donor exchange procedures** your kidney has been donated to an unknown person. When asked about the recipient, please rate for your 'own' recipient. If you don't know the recipient (in **altruistic donation**) you can skip these questions and proceed to the next page.

		Totally disagree	*Disagree*	*Don't agree/ Don't disagree*	*Agree*	*Totally agree*
20.	The quality of life of the recipient has improved due to the donation.	1	2	3	4	5
21.	The disease burden of the recipient in daily life has been reduced.	1	2	3	4	5
22.	The risks for the recipient as a consequence of the kidney disease have been reduced due to the donation.	1	2	3	4	5
23.	My relationship with the recipient has changed for the worse due to the donation.	1	2	3	4	5
24.	The relationship with the recipient has been put under pressure.	1	2	3	4	5
25.	I expected more appreciation and attention from the recipient.	1	2	3	4	5
26.	The recipient is very grateful for the donation.	1	2	3	4	5
27.	Relatives of the recipient (e.g., family members) are very grateful for the donation.	1	2	3	4	5
28.	I'm finding it difficult to let go of my care for the recipient after the donation.	1	2	3	4	5
29.	My relationships with relatives of the recipient have changed for the worse due to the donation.	1	2	3	4	5

REFERENCES

1. Clemens KK, Thiessen-Philbrook H, Parikh CR, et al. Psychosocial health of living kidney donors: a systematic review. Am J Transplant. 2006; 6: 2965-2977.
2. Wirken L, van Middendorp H, Hooghof CW, et al. The Course and Predictors of Health-Related Quality of Life in Living Kidney Donors: A Systematic Review and Meta-Analysis. Am J Transplant. 2015; 15: 3041-3054.
3. Maple H, Chilcot J, Weinman J, Mamode N. Psychosocial Wellbeing after Living Kidney Donation - A Longitudinal, Prospective study. Transpl Int. 2017; 30: 987-1001.
4. Dahm F, Weber M, Muller B, et al. Open and laparoscopic living donor nephrectomy in Switzerland: a retrospective assessment of clinical outcomes and the motivation to donate. Nephrol Dial Transplant. 2006; 21: 2563-2568.
5. Waterman AD, Covelli T, Caisley L, et al. Potential living kidney donors' health education use and comfort with donation. Prog Transplant. 2004; 14: 233-240.
6. Andersen MH, Mathisen L, Veenstra M, et al. Quality of life after randomization to laparoscopic versus open living donor nephrectomy: long-term follow-up. Transplantation. 2007; 84: 64-69.
7. Kok NF, Alwayn IP, Tran KT, Hop WC, Weimar W, Ijzermans JN. Psychosocial and physical impairment after mini-incision open and laparoscopic donor nephrectomy: A prospective study. Transplantation. 2006; 82: 1291-1297.
8. Janki S, Dols LF, Timman R, et al. Five-year follow-up after live donor nephrectomy - cross-sectional and longitudinal analysis of a prospective cohort within the era of extended donor eligibility criteria. Transpl Int. 2017; 30: 266-276.
9. Reese PP, Boudville N, Garg AX. Living kidney donation: outcomes, ethics, and uncertainty. Lancet. 2015; 385: 2003-2013.
10. de Groot IB, Stiggelbout AM, van der Boog PJ, Baranski AG, Marang-van de Mheen PJ, group PA-s. Reduced quality of life in living kidney donors: association with fatigue, societal participation and pre-donation variables. Transpl Int. 2012; 25: 967-975.
11. Fehrman-Ekholm I, Brink B, Ericsson C, Elinder CG, Duner F, Lundgren G. Kidney donors don't regret: follow-up of 370 donors in Stockholm since 1964. Transplantation. 2000; 69: 2067-2071.
12. Schover LR, Streem SB, Boparai N, Duriak K, Novick AC. The psychosocial impact of donating a kidney: long-term follow-up from a urology based center. J Urol. 1997; 157: 1596-1601.
13. Tong A, Chapman JR, Wong G, Kanellis J, McCarthy G, Craig JC. The motivations and experiences of living kidney donors: a thematic synthesis. Am J Kidney Dis. 2012; 60: 15-26.
14. Wiedebusch S, Reiermann S, Steinke C, et al. Quality of life, coping, and mental health status after living kidney donation. Transplant Proc. 2009; 41: 1483-1488.
15. Binet I, Bock AH, Vogelbach P, et al. Outcome in emotionally related living kidney donor transplantation. Nephrol Dial Transplant. 1997; 12: 1940-1948.
16. Frade IC, Fonseca I, Dias L, et al. Impact assessment in living kidney donation: psychosocial aspects in the donor. Transplant Proc. 2008; 40: 677-681.
17. Halverson CM, Wang JY, Poulson M, Karlin J, Crowley-Matoka M, Ross LF. Living Kidney Donors Who Develop Kidney Failure: Excerpts of Their Thoughts. Am J Nephrol. 2016; 43: 389-396.
18. Becerra Perez MM, Menear M, Brehaut JC, Legare F. Extent and Predictors of Decision Regret about Health Care Decisions: A Systematic Review. Med Decis Making. 2016; 36: 777-790.
19. Brehaut JC, O'Connor AM, Wood TJ, et al. Validation of a decision regret scale. Med Decis Making. 2003; 23: 281-292.

20. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004; 240: 205-213.
21. Dutch Transplant Foundation. 2016.
22. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-Item Health Survey 1.0. Health Econ. 1993; 2: 217-227.
23. Vercoulen JH, Swanink CM, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G. Dimensional assessment of chronic fatigue syndrome. J Psychosom Res. 1994; 38: 383-392.
24. Jensen MP, Chen C, Brugger AM. Interpretation of visual analog scale ratings and change scores: a reanalysis of two clinical trials of postoperative pain. J Pain. 2003; 4: 407-414.
25. Corp I. IBM SPSS Statistics. In: In: Windows ISSf e, editor. Version 200 ed. Armonk, New York: IBM CorpReleased 2011.
26. Jacobs CL, Gross CR, Messersmith EE, et al. Emotional and Financial Experiences of Kidney Donors over the Past 50 Years: The RELIVE Study. Clin J Am Soc Nephrol. 2015; 10: 2221-2231.
27. Meyer K, Wahl AK, Bjork IT, Wisloff T, Hartmann A, Andersen MH. Long-term, self-reported health outcomes in kidney donors. BMC Nephrol. 2016; 17: 8.
28. Ralph AF, Butow P, Hanson CS, et al. Donor and Recipient Views on Their Relationship in Living Kidney Donation: Thematic Synthesis of Qualitative Studies. Am J Kidney Dis. 2016; 69: 602-616.
29. Dew MA, Switzer GE, Goycoolea JM, et al. Does transplantation produce quality of life benefits? A quantitative analysis of the literature. Transplantation. 1997; 64: 1261-1273.
30. Lumsdaine JA, Wray A, Power MJ, et al. Higher quality of life in living donor kidney transplantation: prospective cohort study. Transpl Int. 2005; 18: 975-980.

Chapter 4

Pre-donation cognitions of potential living organ donors: The development of the Donation Cognition Instrument (DCI) in potential kidney donors.

Wirken L, van Middendorp H, Hooghof CW, Sanders JSF, Dam RE, van der Pant KAMI, Berendsen ECM, Wellink H, Dackus HJA, Hoitsma AJ, Hilbrands LB, Evers AWM

Nephrology Dialysis Transplantation 2017; 32: 573-580.

ABSTRACT

Background: Cognitions surrounding living organ donation, including the motivation to donate, expectations of donation, and worries about donation, are relevant themes during living donor evaluation. However, there is no reliable psychometric instrument assessing all these different cognitions. This study developed and validated a questionnaire to assess pre-donation motivations, expectations, and worries regarding donation, entitled the Donation Cognition Instrument (DCI).

Methods: Psychometric properties of the DCI were examined using exploratory factor analysis for scale structure and associations with validated questionnaires for construct validity assessment. Results: From seven Dutch transplantation centers, 719 potential living kidney donors were included. The DCI distinguishes cognitions about donor benefits, recipient benefits, idealistic incentives, gratitude, and worries about donation (Cronbach's α .76-.81). Scores on pre-donation cognitions differed with regard to gender, age, marital status, religion, and donation type. With regard to construct validity, the DCI was moderately correlated with expectations regarding donor's personal well-being and slightly to moderately to health-related quality of life.

Conclusions: The DCI is found to be a reliable instrument assessing cognitions surrounding living organ donation, which might add to pre-donation quality of life measures in facilitating psychosocial donor evaluation by healthcare professionals.

INTRODUCTION

According to international guidelines for psychosocial donor evaluation, it is essential for transplant professionals to discuss the motivations and expectations of potential donors, as well as possible worries about donation (1-4). They state that the motivation for donation must be clearly altruistic and genuine, and that the decision to donate must be well-informed and without pressure from the environment (4-6). Further, expectations of the donation should be realistic with regard to transplantation outcomes for the recipient, possible physical consequences for the donor, and possible impact on relationships (1-3). However, psychosocial guidelines do not indicate how to operationalize and assess these cognitions (5).

Generally, the motivation for donation is based on wishing to improve the quality of life of the recipient or being idealistic, based on a feeling of moral duty or religious convictions (7-9). In addition, donors could be motivated by potential personal benefits, such as a higher self-esteem or an increase of their own quality of life due to the improvement of the recipient's health (10, 11).

Previous studies on the expectations of living kidney donors showed that donors generally have quite realistic expectations about the donation, mainly based on personal benefits and on improving the quality of life of the recipient (12-15). Donors generally did not expect gratitude for the donation consisting of financial or symbolic rewards (13).

A small proportion of donors also experiences ambivalence about the donation decision because of worries about temporary limitations due to the surgery, postsurgical pain, their future health, the results of medical examinations, or recipients' health or lifestyle (11, 16-21). In addition, potential donors in kidney exchange procedures have also been found to potentially worry about waiting times, kidney quality equity, and the retraction from reciprocal donation by the donor of a matching couple (22).

Unrealistic cognitions (e.g., unrealistic expectations on recipient outcomes or motivations based on a desire for recognition) could increase the risk of poor psychosocial outcomes after donation, and therefore be a contra-indication.

Most of the limited knowledge on pre-donation cognitions of potential donors is based on qualitative research by means of focus groups or interviews (23) or retrospective assessments (24). Also, some cross-sectional studies have been performed using the Living Donation Expectancies Questionnaire (LDEQ), which focuses on pre-donation expectations of personal well-being after donation (14). These studies have shown that expecting benefits from the donation (e.g., personal growth) is related to higher levels of optimism and worse mental health (14). Although the LDEQ is a valid instrument to assess pre-donation expectations with regard to donor's personal well-being, it does not include either recipient-related expectations or motivations and worries about donation.

Although current guidelines for psychosocial donor evaluation underline the need to assess pre-donation cognitions and mention unrealistic cognitions as a relative or absolute contraindication to donation (25-27), no assessment methods or criteria are provided. Current practice is mainly based on a clinical perspective. Evidence-based instruments to reliably assess pre-donation cognitions would aid clinicians in defining which cognitions could be unrealistic and predictive of adjustment problems after donation. Therefore, the aim of the current study was to develop a short but comprehensive questionnaire to assess different types of pre-donation cognitions (expectancies, motivations, and worries).

MATERIALS AND METHODS

Procedure

A pilot study was conducted in one Dutch transplantation center (Radboud university medical center) in 2010-2011 to develop a new questionnaire on donation cognitions, followed by a multicenter study in seven Dutch transplantation centers (Radboud university medical center, University Medical Center Utrecht, Leiden University Medical Center, University Medical Center Groningen, Maastricht University Medical Center, Academic Medical Center Amsterdam, and VU University Medical Center Amsterdam).

All potential donors attending the first information consultation were invited to participate in the study through an information letter. Exclusion criteria were not being able to read or write the Dutch language and refusal to sign informed consent. After signing informed consent, potential donors who would like to participate in the study were asked if they preferred a paper or a digital format of the questionnaire booklet. The Ethics Committee of the Radboud university medical center decided that the study did not fall under the scope of the Medical Research Involving Human Subjects Act. Therefore, approval by an ethics committee was not indicated for this study, because of the absence of any risk for the participants. In all participating centers, the board approved the execution of the study.

Item generation and scale construction of the donation cognitions questionnaire

Questionnaire items to assess pre-donation cognitions were generated from the literature and clinical practice. The resulting items were judged on comprehensibility and relevance by healthcare professionals and kidney transplantation researchers. In a pilot study, this questionnaire was evaluated by a small group of potential donors to test its feasibility, relevance, and readability. After revision, the final questionnaire consisted of 46 items, of which 28 assessed agreement with statements about different motivations and expectations of donation, including two open response items, measured on a 5-point Likert scale (1=strongly

disagree-5=strongly agree), and 18 items on worries about the donation, including three open response items, measured on a 4-point Likert scale (1=not at all-4=very much).

Other instruments

The following validated questionnaires were used to assess the cross-sectional construct validity of the newly developed questionnaire on pre-donation cognitions.

Donation expectations

Donor expectations regarding personal well-being were assessed by the Living Donation Expectancies Questionnaire (LDEQ) (14). The LDEQ consists of 42 items starting with 'As an organ donor, …', measured on a 5-point Likert Scale (strongly disagree-strongly agree), distinguishing six scales: Interpersonal Benefits (e.g., 'I expect to be respected and admired by family and friends'), Personal Growth (e.g., 'I expect to improve my lifestyle and take better care of my health'), Spiritual Benefits (e.g., 'I expect my donation to be seen as a way of honoring my God'), Quid Pro Quo (e.g., 'I expect preferential treatment by the recipient after donation'), Health Consequences (e.g., 'I expect to experience a great deal of pain and discomfort'), and Miscellaneous Consequences (e.g., 'I expect to have more financial problems'). Higher scores represent higher expectations in that domain. Cronbach's alpha in the present study varied between .65 (Quid Pro Quo and Miscellaneous Consequences) and .93 (total LDEQ).

Health-related quality of life (HRQoL)

Physical functioning: The physical functioning of potential donors was assessed by the Physical Health Composite score and its subscales of the RAND Short Form-36 Health Status Inventory (RAND SF36) (28) and the short version of the Checklist Individual Strength-Fatigue (CIS) (29, 30). The RAND SF36 is a widely used 36-item questionnaire assessing eight aspects of HRQoL, of which four assess physical health and are summarized into a composite score: Physical Functioning, Role Limitations due to Physical Health Problems, Pain, and General Health Perceptions. The Hays norm-based scoring algorithm was applied, using item response theory with raw scores being transformed into T-scores with an average of 50 and a standard deviation of 10 in the general population (28). Higher scores represent better HRQoL. Cronbach's alpha varied between .61 (General Health Perceptions) and .86 (Role Limitations due to Physical Health Problems). The short version of the CIS assesses fatigue by means of 4 items (e.g., 'I feel tired') on a 7-point scale (1=strongly agree 7=strongly disagree). Higher scores represent more fatigue. Cronbach's alpha was .86.

Psychological functioning: The psychological functioning of potential donors was assessed using the RAND SF36 Mental Health Composite and its subscales (28), the Hospital Anxiety and Depression Scale (HADS) (31), and neuroticism as assessed with the NEO Personality Inventory-Revised (NEO-PI-R) (32, 33).

Of the RAND SF36, four subscales assess mental health, which are summarized into a composite score: Emotional Well-being, Role Limitations due to Emotional Problems, Social Functioning, and Energy (28). Cronbach's alphas varied between .71 (Social Functioning) and .87 (Mental Health Composite). The HADS is a widely used, short screening questionnaire for symptoms of anxiety and depression (31), consisting of two seven-item subscales with a score range of 0 to 21. Higher scores represent more anxiety or depression. Cronbach's alpha varied between .73 (Depression) and .83 (total HADS). The NEO-PI-R assesses the personality characteristic of neuroticism by means of eight items on a 5-point Likert scale (32, 33). Higher scores represent higher sensitivity for stressful situations. Cronbach's alpha was .77.

Social-relational functioning: Social-relational functioning of donors was assessed with the Interpersonal Sensitivity Measure (IPSM) (34) and the Inventory for Social Reliance (ISR) (35). Two subscales of the IPSM were used, Interpersonal Awareness (7 items; e.g., 'I worry about the effect I have on other people') and Timidity (8 items; e.g., 'I will do something I do not want to do rather than offend or upset someone') (34). Scores were rated on a 4-point Likert scale, with higher scores representing more interpersonal awareness and timidity. Cronbach's alpha was .80 for Interpersonal Awareness and .65 for Timidity. The Perceived Support scale of the ISR assessed the level of perceived social support by means of 5 items, rated on a 4-point Likert scale, with higher scores representing better interpersonal functioning (36). Cronbach's alpha was .87.

Statistical analyses

Not normally distributed scales were transformed with (reflected) logarithmic transformations. The suitability of the data for principal component analysis was evaluated by the Barlett's Test of Sphericity (37) and Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy (38, 39). Two Principal Component Exploratory Factor Analyses with Promax rotation and Kaiser Normalization for scale structure assessment were conducted, one on donor motivation and expectation items and one on the items on donor worries, as these were formulated and scored distinctively. The selection of factors was based on the Eigenvalues, Cattell's scree test, and factor interpretability. Of the resulting factors, internal consistency was assessed by Cronbach's α. Factors were transformed into subscale scores by averaging the included items when at least two-third of the items were filled in. To examine whether cognitions about donation were associated with demographic and donation-related characteristics, depending on the measurement level, correlational analyses (e.g., age), Independent Samples T-tests (using Welch's t-test in case of violation of homogeneity of variances) (e.g., marital status), or One-Way Analyses of Variance (e.g., educational level) were conducted. Pearson and Spearman correlation coefficients with the LDEQ and HRQoL were calculated for construct validity. A p-value below .05 was considered significant. Data analyses were conducted using IBM SPSS Statistics 20.0 (40).

RESULTS

Participant characteristics

The questionnaire was sent to 940 potential donors, of which 719 were returned (response rate: 76%). The majority (57%) of the 221 potential donors not returning the questionnaire withdrew from the donation procedure because of medical reasons (58%), preference for another living donor (20%), donor personal reasons (17%), or availability of a post-mortal donor (6%). Demographic characteristics did not differ between participants and refusers (Table 1). Both sexes were almost equally represented in the study (57% was female), the mean age of the participants was 54.2 (SD=11.4; range 19-76) years, and most had secondary level education (64.4%). The majority (79.6%) intended to donate directly to a recipient they knew.

Table 1. Demographic characteristics of the potential donors (N=719)

Characteristic	Mean ± sd (range) N (%)
Age Mean ± sd (range)	54.2 ± 11.4 (19-76)
Gender (% female)	57%
Marital status[a]	
Single	21.7%
With partner	78.3%
Educational level[a]	
Primary education	4.8%
Secondary education	64.4%
Tertiary education	30.8%
Donation type	
Direct	79.6%
Kidney exchange procedure	12.2%
Anonymous	8.2%
Donor-recipient relationship	
Spouse	29.3%
Parent	17.9%
Sibling	18.5%
Child	5.6%
Other - related	4.3%
Other - unrelated	16.1%
Anonymous	8.2%
Being religious[a]	52.4%

[a] added after pilot study (n = 624)
Values given are mean ± SD or percentages

Exploratory principal component analysis of the donation cognitions questionnaire

Donation Cognition Instrument-Motivation and Expectations (DCI-ME)

Principal component analysis was permitted (KMO=.75, Bartlett $p<.001$) on the 25 items assessing donor motivations and expectations (the item 'I have no specific expectations of the donation' was excluded from analysis and the two open response options did not indicate any relevant missing motivations and expectations). Based on factor loadings below .40 or cross-loadings of more than .20, three items were excluded from the final questionnaire, resulting in the 22-item Donation Cognition Instrument- Motivation and Expectations (DCI-ME) (Table 2). Four factors were distinguished, explaining a total variance of 52.8%, namely Donor Benefits (7 items, cognitions on improving donor's own well-being), Recipient Benefits (6 items, cognitions on improving recipient's well-being), Idealistic Incentives (6 items, cognitions about living according to one's ideals or religious convictions), and Gratitude (3 items, cognitions on expressions of gratitude from the recipient or others). Scales were normally distributed, except for the Recipient Benefits scale, which was transformed using reflected logarithmic transformation. Descriptive statistics are presented in Table 2, showing cognitions about Recipient Benefits being most commonly reported (M=4.57, SD=0.4 on a 5-point scale) and cognitions about Donor Benefits least commonly (M=1.96, SD=0.7). The internal consistency varied between .76 and .81. Intercorrelations between the subscales revealed non-significant to moderate associations ($.14 \leq r. \leq 30$).

Table 2. Principal Components Analysis with Promax Rotation on the Donation Cognition Instrument–Motivations and Expectations (DCI-ME) (n=719)[a]

Item[b]		Donor Benefits	Recipient Benefits	Idealistic Incentives	Gratitude
Factor I			**Factor loadings**		
5	I wish to improve my relationship with the recipient through the donation.	**0.81**	-0.02	-0.09	0.04
6	I wish to improve my relationship with others (for instance family members of the recipient) through the donation.	**0.73**	-0.13	0.01	0.03
19	I expect my relationship with the recipient to improve as a result of the donation.	**0.73**	-0.08	-0.04	0.20
20	I expect my relationship with family members/ friends (for example of the recipient) to improve as a result of the donation.	**0.70**	-0.11	0.08	0.17
4	I wish to donate in order to improve the quality of my own life.	**0.70**	0.28	-0.06	-0.28
18	I expect my own quality of life to improve as a result of the donation.	**0.68**	0.21	0.04	-0.16
24	I expect to receive a contribution (immaterial or symbolic) for the donation.	**0.45**	-0.14	0.03	0.17

Table 2. Principal Components Analysis with Promax Rotation on the Donation Cognition Instrument–Motivations and Expectations (DCI-ME) (n=719)[a] (continued)

Item[b]		Donor Benefits	Recipient Benefits	Idealistic Incentives	Gratitude
Factor II					
17	I expect the health risks for the recipient to decrease significantly as a result of the donation.	0.02	**0.71**	-0.08	0.19
16	I expect the disease burden of the recipient in everyday life to decrease significantly.	0.04	**0.70**	-0.15	0.21
3	I wish to donate in order to reduce the health risks for the recipient.	-0.03	**0.66**	0.11	-0.13
2	I wish to donate in order to reduce the disease burden of the recipient in everyday life.	-0.03	**0.65**	0.12	-0.04
1	I wish to donate in order to improve the quality of life of the recipient.	-0.10	**0.61**	0.14	-0.11
15	I expect the quality of life of the recipient to improve greatly.	-0.02	**0.61**	-0.21	0.36
Factor III					
11	I wish to make a contribution to a better world.	0.08	-0.06	**0.72**	0.03
10	I am acting in accordance with my religion or beliefs.	0.02	0.00	**0.71**	-0.17
12	Other donors are an example for me of love for one's fellow humans.	0.03	0.07	**0.68**	0.12
13	I am glad to be able to help someone.	-0.16	0.17	**0.60**	0.11
25	I expect to be strengthened in my religious or other beliefs as a result of the donation.	0.24	-0.12	**0.50**	0.00
26	I expect that I will serve as a good example for others through the donation.	0.07	0.07	**0.48**	0.29
Factor IV					
23	I expect relatives of the recipient to be very grateful for the donation.	0.04	-0.05	0.10	**0.83**
22	I expect the recipient to be very grateful for the donation.	0.06	0.00	0.03	**0.82**
21	I expect that as a result of the donation, I will be able to make a real difference for the recipient.	0.03	0.18	0.08	**0.55**
Excluded items					
7	I wish to help a stranger/ acquaintance/friend/ family member.	-0.26	-0.06	0.42	0.16
8	I am doing this out of love for the recipient.	0.11	0.36	0.18	-0.19
9	I find it self-evident to do this for a fellow human being.	-0.03	0.30	0.41	-0.04
	Mean (sd) (range 1-5)[c]	1.96 (0.72)	4.57 (0.41)	2.87 (0.84)	3.44 (1.03)
	Cronbach's alpha	.81	.78	.76	.77
	% Variance explained	22.1	13.9	8.9	7.9

[a] factor loadings on corresponding factors are in boldface type

[b] item number of original questionnaire, with item 14 and 26 being open response items

[c] higher means correspond with more cognitions in that domain

Donation Cognition Instrument-Worries (DCI-W)

Principal component analysis was permitted (KMO=.73, Bartlett $p<.001$) on the 15 donor worries about themselves, the recipient, or future relationship changes (the three open response options did not indicate relevant missing worries). Five items were excluded for having a kurtosis higher than 10 ('I am worried about the reaction of my relatives to the donation'; 'I am worried that my relationship with the recipient will deteriorate'; 'I am worried that there will be more pressure and more tension in the relationship'; 'I am worried that the relations within the family and/or relationship will change for the worse following the donation'; 'I am worried that the division of roles within the family and/or relationship will change for the worse following the donation'). One item had a factor loading below .40, resulting in a 9-item Donation Cognition Instrument-Worries (DCI-W) (Table 3). One factor could be distinguished, which was normally distributed after logarithmic transformation, explaining a total variance of 33.5%. Donors in general reported minimal worries about the donation (M=1.47, SD=0.3 on a 4-point scale). The internal consistency was .74. Non-significant to small correlations between the DCI-W and subscales of the DCI-ME were found (r-values varying from .04 to .18).

Table 3. Principal Components Analysis with Promax Rotation on the Donation Cognition Instrument–Worries (DCI-W) (n=719)[a]

	Item[b]	Worries about the donation
Factor I		**Factor Loadings**
3	I am worried about the operation.	**0.72**
4	I am worried about the physical consequences of the donation, such as a possible infection or pain.	**0.70**
7	I am worried that the kidney will be rejected by the recipient.	**0.64**
10	I am worried about the high expectations of the recipient regarding the transplant.	**0.57**
9	I am worried that the recipient will have the idea that s/he should always remain grateful.	**0.53**
2	I am worried about the results of the medical tests.	**0.51**
5	I am worried about the reaction of my partner and/or children to the donation.	**0.51**
1	I am worried that I will feel guilty if I decide not to go ahead with the donation.	**0.49**
12	I am worried that there will be constant pressure to be grateful.	**0.46**
Excluded item		
8	I am worried about the lifestyle of the recipient after the transplant, for instance smoking or engaging in risky sports.	0.31
	Mean (sd) (range 1-4)[c]	1.47 (0.33)
	Cronbach's alpha	.74
	% Variance explained	33.5

[a] factor loadings on corresponding factor are in boldface type

[b] item number of original questionnaire, as stated on page 12, 5 items were not included in the PCA

[c] higher means correspond with more worrying

Table 4. Relationship of pre-donation cognitions with demographic and donation-related variables

	Donor Benefits				Recipient Benefits				Idealistic Incentives				Gratitude				Worries			
	Mean [ab]	F	t	*p* [c]	Mean [ab]	F	t	*p* [c]	Mean [ab]	F	t	*p* [c]	Mean [ab]	F	t	*p* [c]	Mean [ab]	F	t	*p* [c]
Gender																				
Male	2.02	6.06	1.82	.08	4.57	1.61	-0.46	.64	2.84	0.92	-0.82	.41	3.71	7.02	6.35	<.001***	1.46	0.64	-1.31	.19
Female	1.92				4.56				2.90				3.24				1.49			
Marital Status																				
Single	1.82	0.11	-2.37	.02*	4.57	0.28	0.13	.90	2.93	0.06	1.05	.30	3.31	6.05	-1.57	.12	1.46	0.05	-0.79	.43
Steady partner	1.99				4.57				2.85				3.48				1.49			
Educational Level																				
Primary	2.25	2.53		.08	4.43	1.61		.20	2.99	1.76		.17	3.85	2.31		.10	1.45	0.51		.60
Secondary	1.96				4.59				2.89				3.42				1.48			
Tertiary	1.93				4.55				2.77				3.46				1.49			
Donation Type																				
Direct	1.98	1.48		.23	4.57	0.13		.88	2.82	9.96		<.001***	3.44	1.16		.31	1.48	0.06		.94
Kidney exchange procedure	1.99				4.58				2.90				3.35				1.47			
Anonymous	1.81				4.55				3.33				3.61				1.45			
Being religious																				
Yes	2.01	2.58	-2.01	.045*	4.58	0.82	0.77	.45	3.08	0.51	-6.96	<.001***	3.45	0.00	-0.26	.80	1.48	0.70	0.25	.80
No	1.89				4.56				2.63				3.43				1.48			

[a] higher scores correspond to more cognitions in that domain

[b] Donor Benefits (range 1-5), Recipient Benefits (range 1-5), Idealistic Incentives (range 1-5), Gratitude (range 1-5), Worries (range 1-4)

[c] *p<.05, **p<.01, ***p<.001

Table 5. Correlation coefficients of the Donation Cognition Instrument subscales DCI-ME and DCI-W with validated questionnaires [ab]

	DCI-ME				DCI-W
	Donor Benefits	**Recipient Benefits**	**Idealistic Incentives**	**Gratitude**	**Worries about donation**
Living Donation Expectancies Questionnaire (LDEQ)					
Interpersonal Benefit	.47***	-.03	.32***	.37***	.32***
Personal Growth	.44***	.07	.37***	.28***	.28***
Spiritual Benefit	.38***	.06	.52***	.23***	.14**
Quid pro Quo	.45***	-.02	.26***	.35***	.26***
Health Consequences	.34***	-.17***	.12**	.15**	.43***
Miscellaneous Consequences	.21***	-.23***	.13**	.01	.30***
Physical Functioning					
RAND Short Form-36 Health Status Inventory (RAND SF36)					
Physical Functioning	.00	.07	.01	.08*	-.10**
Role Limitations - Physical Health Problems[c]	-.14***	.00	-.02	-.08*	-.15***
Pain	.00	.07	.01	.03	-.15***
General Health Perceptions	-.07	.11**	.03	.04	-.29***
Physical Health Composite	-.06	.10**	.03	.04	-.26***
Short CIS Fatigue					
Fatigue	.09*	-.11**	-.09*	-.07	.30***
Psychological functioning					
RAND Short Form-36 Health Status Inventory (RAND SF36)					
Emotional Well-being	-.13**	.12**	-.02	.04	-.37***
Role Limitations - Emotional Problems[c]	-.05	.08*	.02	.05	-.14***
Energy/Fatigue	-.05	.12**	.05	.04	-.32***
Social Functioning	-.09*	.05	-.07	-.01	-.32***
Mental Health Composite	-.09*	.13**	.00	.03	-.37***
Hospital Anxiety and Depression Scale (HADS)					
Anxiety	.12**	-.07	.02	.04	.44***
Depression	.10**	-.10**	-.05	.01	.24***
Social-relational functioning					
NEO Personality Inventory–Revised (NEO PI R)					
Neuroticism - Vulnerability	.15***	-.16***	-.02	-.01	.35***
Interpersonal Sensitivity Measure (IPSM)					
Interpersonal Awareness	.12**	-.07	.05	.04	.42***
Timidity	.08*	-.06	.12**	.03	.27***
Inventory for Social Reliance (ISR)					
Perceived Support	-.06	.08*	-.01	-.04	-.18***

[a] DCI-ME: Donation Cognition Instrument - Motivations and Expectations; DCI-W: Donation Cognition Instrument- Worries (higher scores correspond to more cognitions in that domain); LDEQ: Living Donation

Expectancies Questionnaire (higher scores correspond to more expectations on that domain); RAND SF36: RAND Short Form-36 Health Status Inventory (higher scores correspond to better HRQoL); CIS, Checklist Individual Strength (higher scores correspond to more fatigue); HADS, Hospital Anxiety and Depression Scale (higher scores correspond to more anxiety or depression); NEO PI-R, NEO Personality Inventory – Revised (higher scores correspond to more neuroticism); IPSM, Interpersonal Sensitivity Measure (higher scores correspond to more interpersonal sensitivity); ISR, Inventory for Social Reliance (higher scores correspond to better interpersonal functioning)

[b] $^{*}p<.05$, $^{**}p<.01$, $^{***}p<.001$

[c] Spearman correlation coefficients

Relationship of pre-donation cognitions with demographic and donation-related variables

Significantly higher scores on donor benefit cognitions were reported by potential donors with a steady partner ($t(609)=-2.37$, $p=.02$), and those with a religious conviction ($t(610)=-2.01$, $p=.045$). Higher scores on recipient benefit cognitions were associated with a higher age ($r=.08$, $p=.04$). More idealistic incentives were reported by religious ($t(612)=-6.96$, $p<.001$) and anonymous ($F(2,706)=9.96$, $p<.001$) potential donors. Expectations of gratitude were reported more by males than females ($t(691.52)=6.35$, $p<.001$). No significant associations were found between worries about donation and demographic or donation-related variables (p-values>.19) (Table 4).

Construct validity of the Donation Cognition Instrument

Correlation coefficients of the DCI with the only other questionnaire assessing pre-donation expectations (LDEQ) and HRQoL measures are presented in Table 5. Correlations between the DCI and LDEQ subscales were mostly moderate (40% of correlation coefficients between .30-.50) or small (40% between .10-.30), whereas only non-significant (67% between .00-.10) to small correlations (33%) were found for the recipient benefits subscale of the DCI and the LDEQ. Higher scores on donor benefit cognitions showed small associations with worse psychological and social-relational functioning. Higher scores on recipient benefit cognitions were slightly associated with better physical and psychological functioning. More idealistic incentives showed only a small association with more timidity, whereas correlations for gratitude did not reach the .10 threshold. More worries showed moderate correlations with worse psychological and social-relational functioning, and small correlations with worse physical functioning.

DISCUSSION

Guidelines for psychosocial donor evaluation advise an appraisal of cognitions regarding the donation, including donor motivation, expectations, and worries about donation.

However, no instruments or criteria on how to judge these cognitions are provided. To meet this need, the Donation Cognition Instrument was developed. Five factors could be distinguished, measuring cognitions regarding donors' own HRQoL improvement (Donor Benefits), recipient's wellbeing improvement (Recipient Benefits), living according to one's ideals or religious convictions (Idealistic Incentives), expectations of gratitude in exchange for donation (Gratitude), and donation worries. Reliability of the DCI was verified by high internal consistency. Validity of the DCI was supported by small to moderate relationships with pre-donation cognitions and HRQoL, supporting the potential added value of the DCI for psychosocial evaluation in potential living organ donors.

Pre-donation motivations and expectations were mainly based on improving the recipient's health, which is in line with previous research showing that donors are more focused on recipient's functioning than on their own health (9). Expectations of gratitude for donation were also common. Potential donors mentioned their own HRQoL improvement less often as a primary motivation to donate, and generally indicated few worries about the consequences of donation. This may be due to the fact that the questionnaires were completed at the beginning of the donor evaluation procedure, when the wish to donate dominates. Possibly, worries about surgery or recipient outcomes arise later when the surgery is planned.

Gender differences on pre-donation cognitions were found, with males expecting more gratitude for donation. This is in line with research on the existing expectancies questionnaire (LDEQ), which found men to score higher on the subscale Quid Pro Quo, which also encompasses expecting something in return for the donation (14). Further, religious and anonymous donors reported more idealistic motivations. This was to be expected due to the presence of religious convictions in this scale and the fact that anonymous donors have been found to donate out of their ideals with regard to helping others (24, 41).

The validation of the DCI with the other validated questionnaire on pre-donation expectations regarding donor's personal well-being (LDEQ) (14) showed a small to moderate overlap between most subscales. The low associations between recipient benefit cognitions and the LDEQ subscales indicate that the previous instrument does not yet assess these cognitions. Considering that they were the most often reported donor motivations or expectations and were related to better pre-donation HRQoL supports the potential value of this new, more encompassing instrument. To provide first indications that the DCI measures something additional to HRQoL, validity was assessed between the DCI and physical, psychological, and social-relational functioning. More worries were moderately associated with a worse pre-donation HRQoL. This is in line with research showing that HRQoL is related to worrying in other health conditions (42). The overall small associations between pre-donation cognitions and HRQoL support the notion of unique dimensions of potential donor's attitudes being assessed by the DCI.

Strengths of the current study include the large sample from seven transplantation centers, the use of validated questionnaires, and the applicability of the questionnaire for other donor populations due to the generalized formulation of items. The generalizability of the results is limited to the Dutch living kidney donor population and needs to be confirmed in alternative donor populations from other countries. Further, because the questionnaires were administered at the beginning of the donor evaluation, responses might be influenced by social desirability to positively influence healthcare professionals in the donation decision (8). Last, recent studies indicate that non-altruistic donor motives and expectations about finances and insurance are relevant themes for donor evaluation that are currently not included in the DCI. Future studies could add items on these themes to optimize the DCI.

At this moment no golden standard or longitudinal studies on donor cognitions are available, and possible risk or resilience factors for longer-term donor functioning are not yet clearly defined. Therefore, no valid cutoff criteria for the DCI could be formulated based on this cross-sectional study. Future prospective studies should examine the potential of the DCI to predict longer-term adjustment problems in living donors and to identify unfavorable cognitions that are contra-indications for donor eligibility (1, 27). Through this, donors who might benefit from psychosocial interventions could be identified. However as a first step in this process, the construct validity indices used in this study indicate the potential of the DCI to systematically assess pre-donation cognitions in clinical practice that might add to existing questionnaires on donor expectations and HRQoL. Further, the DCI could provide potential donors more insight into their own motivations, expectations, and worries and might aid in the process of donation decision-making. Lastly, it could offer discussion themes for healthcare professionals during donor evaluation consultation, when potential donors report unfavorable motivations, unrealistic expectations or excessive worries about donation. In these cases, means and standard deviations provided from current study could be used as norm scores, because of the large and representative sample that was used. To conclude, the Donation Cognition Instrument is a reliable instrument to assess pre-donation cognitions, which has the potential to become part of the psychosocial donor evaluation to aid donor decisions and suggest donor intervention needs.

REFERENCES

1. Duerinckx N, Timmerman L, Van Gogh J, et al. Predonation psychosocial evaluation of living kidney and liver donor candidates: a systematic literature review. Transpl Int. 2014; 27: 2-18.
2. NHMRC. Organ and tissue donation by living donors. Guidelines for ethical practice for health professionals. Canberra; 2007.
3. Andrews PA, Burnapp L, Manas D, et al. Summary of the British Transplantation Society/Renal Association U.K. guidelines for living donor kidney transplantation. Transplantation. 2012; 93: 666-673.
4. Venkat KK, Eshelman AK. The evolving approach to ethical issues in living donor kidney transplantation: a review based on illustrative case vignettes. Transplant Rev. 2014; 28: 134-139.
5. Tong A, Chapman JR, Wong G, de Bruijn J, Craig JC. Screening and follow-up of living kidney donors: a systematic review of clinical practice guidelines. Transplantation. 2011; 92: 962-972.
6. van Hardeveld E, Tong A, Cari. The CARI guidelines. Psychosocial care of living kidney donors. Nephrology. 2010; 15 Suppl 1: S80-S87.
7. Fehrman-Ekholm I. View from a living donor. Clin Transplant. 2013: 181-186.
8. Hildebrand L, Melchert TP, Anderson RC. Impression management during evaluation and psychological reactions post-donation of living kidney donors. Clin Transplant. 2014; 28: 855-861.
9. Lennerling A, Forsberg A, Meyer K, Nyberg G. Motives for becoming a living kidney donor. Nephrol Dial Transplant. 2004; 19: 1600-1605.
10. Clemens KK, Thiessen-Philbrook H, Parikh CR, et al. Psychosocial health of living kidney donors: a systematic review. Am J Transplant. 2006; 6: 2965-2977.
11. Lennerling A, Forsberg A, Nyberg G. Becoming a living kidney donor. Transplantation. 2003; 76: 1243-1247.
12. de Groot IB, Schipper K, van Dijk S, et al. Decision making around living and deceased donor kidney transplantation: a qualitative study exploring the importance of expected relationship changes. BMC Nephrol. 2012; 13: 103-114.
13. Tong A, Chapman JR, Wong G, Kanellis J, McCarthy G, Craig JC. The motivations and experiences of living kidney donors: a thematic synthesis. Am J Kidney Dis. 2012; 60: 15-26.
14. Rodrigue JR, Guenther R, Kaplan B, Mandelbrot DA, Pavlakis M, Howard RJ. Measuring the expectations of kidney donors: initial psychometric properties of the Living Donation Expectancies Questionnaire. Transplantation. 2008; 85: 1230-1234.
15. Rodrigue JR, Paek M, Whiting J, et al. Trajectories of perceived benefits in living kidney donors: association with donor characteristics and recipient outcomes. Transplantation. 2014; 97: 762-768.
16. Agerskov H, Bistrup C, Ludvigsen MS, Pedersen BD. Living kidney donation: considerations and decision-making. Journal of renal care. 2014; 40: 88-95.
17. Dahm F, Weber M, Muller B, et al. Open and laparoscopic living donor nephrectomy in Switzerland: a retrospective assessment of clinical outcomes and the motivation to donate. Nephrol Dial Transplant. 2006; 21: 2563-2568.
18. Lumsdaine JA, Wray A, Power MJ, et al. Higher quality of life in living donor kidney transplantation: prospective cohort study. Transpl Int. 2005; 18: 975-980.
19. Agerskov H, Ludvigsen MS, Bistrup C, Pedersen BD. Living kidney donors' experiences while undergoing evaluation for donation: a qualitative study. J Clin Nurs. 2015; 24: 2258-2267.
20. Waterman AD, Covelli T, Caisley L, et al. Potential living kidney donors' health education use and comfort with donation. Progress in transplantation. 2004; 14: 233-240.

21. Pradel FG, Mullins CD, Bartlett ST. Exploring donors' and recipients' attitudes about living donor kidney transplantation. Progress in transplantation. 2003; 13: 203-210.
22. Rodrigue JR, Leishman R, Vishnevsky T, Evenson A, Mandelbrot DA. Concerns of ABO incompatible and crossmatch-positive potential donors and recipients about participating in kidney exchanges. Clin Transplant. 2015; 29: 233-241.
23. Yi M. Decision-making process for living kidney donors. J Nurs Scholarsh. 2003; 35: 61-66.
24. Maple H, Chilcot J, Burnapp L, et al. Motivations, outcomes, and characteristics of unspecified (nondirected altruistic) kidney donors in the United Kingdom. Transplantation. 2014; 98: 1182-1189.
25. Abecassis M, Adams M, Adams P, et al. Consensus statement on the live organ donor. JAMA. 2000; 284: 2919-2926.
26. Dew MA, Jacobs CL, Jowsey SG, et al. Guidelines for the psychosocial evaluation of living unrelated kidney donors in the United States. Am J Transplant. 2007; 7: 1047-1054.
27. Rodrigue JR, Pavlakis M, Danovitch GM, et al. Evaluating living kidney donors: relationship types, psychosocial criteria, and consent processes at US transplant programs. Am J Transplant. 2007; 7: 2326-2332.
28. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-Item Health Survey 1.0. Health Econ. 1993; 2: 217-227.
29. Alberts M, Smets EM, Vercoulen JH, Garssen B, Bleijenberg G. Abbreviated fatigue questionnaire: a practical tool in the classification of fatigue. Ned Tijdschr Geneeskd. 1997; 141: 1526-1530.
30. Vercoulen JH, Swanink CM, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G. Dimensional assessment of chronic fatigue syndrome. J Psychosom Res. 1994; 38: 383-392.
31. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983; 67: 361-370.
32. Costa PT, Jr., & McCrae, R. R. The NEO Personality Inventory manual. Odessa: Psychological Assessment Resources; 1985.
33. Hoekstra HA, Ormel, J. & de Fruyt F. NEO PI R. Big Five Personality Questionnaires. Amsterdam: Hogrefe 1996.
34. Boyce P, Parker G. Development of a scale to measure interpersonal sensitivity. Aust N Z J Psychiatry. 1989; 23: 341-351.
35. Dam-Baggen RKF. De Inventarisatielijst Sociale Betrokkenheid (ISB): een zelfbeoordelingslijst om sociale steun te meten (Inventory for social reliance (ISR): a self-report inventory for the measurement of social support). Gedragstherapie. 1992; 25: 27-46.
36. van Dam-Baggen RKF. Assessing Social Anxiety: The Inventory of Interpersonal Situations (IIS). Eur J Psychol Assess. 1999; 15: 25-38.
37. Bartlett MS. A note on the multiplying factors for various chi square approximations. J R Stat Soc. 1954; 16 (Series B): 296-298.
38. Kaiser H. A second generation Little Jiffy. Psychometrika. 1970; 35: 401-415.
39. Kaiser H. An index of factorial simplicity. Psychometrika. 1974; 39: 31-36.
40. IBM SPSS Statistics. IBM Corp. Released 2011. In: Windows ISSf, editor. Version 20.0 ed. Armonk, New York: IBM Corp.
41. Massey EK, Kranenburg LW, Zuidema WC, et al. Encouraging psychological outcomes after altruistic donation to a stranger. Am J Transplant. 2010; 10: 1445-1452.
42. Hyphantis T, Kotsis K, Tsifetaki N, et al. The relationship between depressive symptoms, illness perceptions and quality of life in ankylosing spondylitis in comparison to rheumatoid arthritis. Clin Rheumatol. 2013; 32: 635-644.

Chapter 5

Combining transplant professional's psychosocial evaluation and donor self-report measures to optimize the prediction of HRQoL after kidney donation: a prospective multicenter study

Wirken L, van Middendorp H, Hooghof CW, Sanders JSF, Dam RE, van der Pant KAMI, Wierdsma JM, Wellink H, Ulrichts PTR, Hoitsma AJ, Hilbrands LB, Evers AWM

Submitted for publication.

ABSTRACT

The psychosocial evaluation of kidney donor candidates relies mostly on the clinical viewpoint of transplant professionals, because evidence-based guidelines for donor eligibility are currently lacking. However, the accuracy of these clinical risk judgments is as yet unknown. Therefore, the current prospective multicenter study examined the effectiveness of the psychosocial evaluation by transplant professionals and the potential value of donor self-report measures in optimizing the donor evaluation. The predictive value of pre-, intra-, and post-donation factors to impaired longer-term health-related quality of life (HRQoL) of kidney donors was studied. Transplant professionals (nephrologists, coordinating nurses, social workers, and psychologists) filled in risk estimation questionnaires on kidney donor candidates. Further, 230 kidney donors from seven Dutch transplantation centers completed questionnaires (e.g., on HRQoL) before, and 6 and 12 months after donation. Both higher risk judgments of transplant professionals and donor self-report measures, particularly of poorer baseline physical and psychological functioning, significantly predicted impaired longer-term HRQoL after donation. This endorses the effectiveness of the psychosocial donor evaluation by professionals, and the additional value of donor self-report measures in optimizing the psychosocial evaluation. Consequently, donor eligibility decisions could be more reliable and tailored interventions for donors at risk could be provided.

INTRODUCTION

The recent increase in the number of living donor kidney transplantations has led to more research on donor wellbeing, including donor decision-making (e.g., motivation, expectations, and worries) and health-related quality of life (HRQoL) (1-7). Previous research indicates that most donors recover well after surgery. However, a subgroup of donors experiences sustained HRQoL difficulties (2, 6), potentially caused by donor or recipient complications (8-10), unmet donation expectations (11, 12), or social-relational problems (13). An accurate psychosocial evaluation enables the early identification of problems and the provision of counseling to prevent donation-related difficulties (14). Currently, evidence-based guidelines for psychosocial eligibility screening are scarce (15, 16), because only little research is available on predictors for longer-term HRQoL using baseline, intra- and post-operative measures (17-19). The most consistent risk factor of impaired HRQoL after donation has been poor baseline psychological functioning (6), whereas limited evidence has been found for a broad range of demographic, medical, and psychosocial risk factors, including being single, donor complications, and recipient functioning (4, 20, 21). Because of the lack of large prospective prediction studies, the psychosocial donor evaluation relies mostly on the clinical viewpoint of transplant professionals. However, the accuracy of these clinical judgments is as yet unknown. Also, procedures are not consistent across donation programs (22). A standardized evidence-based psychosocial evaluation would enable transparent eligibility decisions and interventions for donors with a high-risk profile, but more knowledge about the most important predictors of poor HRQoL after donation is necessary.

Summarizing, due to a shortage of large prospective prediction studies, psychosocial donor screening is currently mainly based on clinical risk assessments. The accuracy of these clinical judgments of transplant professionals and the possible value of donor self-report measures in eligibility screening must be examined. The current prospective study examines the value and relative contribution of risk estimations by transplant professionals, donor self-report measures, and pre-, intra-, and post-donation factors in predicting both short- and longer-term HRQoL of kidney donors.

MATERIALS AND METHODS

Procedure

All potential donors from seven Dutch transplantation centers (Radboud university medical center, University Medical Center Groningen, Leiden University Medical Center, Academic Medical Center Amsterdam, University Medical Center Utrecht, VU University Medical Center Amsterdam, and Maastricht University Medical Center) were invited to

participate in the study after their first screening visit (2011-2015). Transplant professionals routinely involved in donor evaluation (nephrologists, coordinating nurses, social workers, and psychologists) filled in a short questionnaire on their risk estimation for poorer donor HRQoL after donation. Also, potential donors completed a screening questionnaire either by email or on paper. If donation took place, donors received a similar questionnaire six and twelve months after surgery. Illiteracy was the only exclusion criterion. The Radboud university medical center Ethics Committee decided that the study did not fall under the scope of the Medical Research Involving Human Subjects Act. Therefore, approval by an ethics committee was not indicated, because of the absence of any risk for the participants. In all participating centers, the board approved the study. All participants signed informed consent. The clinical and research activities being reported are consistent with the Declaration of Helsinki and the Declaration of Istanbul.

Participants

Transplant professionals

On 533 potential donors (91% of participating donors), 1,048 risk estimation questionnaires were completed by coordinating nurses (n=489), medical social workers (n=339), nephrologists (n=201), and psychologists (n=19).

Potential donors

In total, 588 potential donors participated (75% response rate), of whom 361 (61%) actually donated a kidney. The mean time between screening and donation was 7.0±5.2 months (range 1-39 months). Reasons for exclusion from the donation procedure are presented in Figure 1. Complete data of 230 donors were available, excluding participants filling out the questionnaires more than three months after the intended time (Figure 1).

Measures

Predictor variables

Demographic and pre-, intra- and post-operative health characteristics

Donor demographic characteristics as well as pre-, intra- and post-operative health characteristics (e.g., physical comorbidity, hospital stay, complications) were assessed. Data on recipient's pre-transplantation treatment and post-transplantation outcome (i.e., graft failure or death) were derived from the Dutch Organ Transplantation Registration system (23).

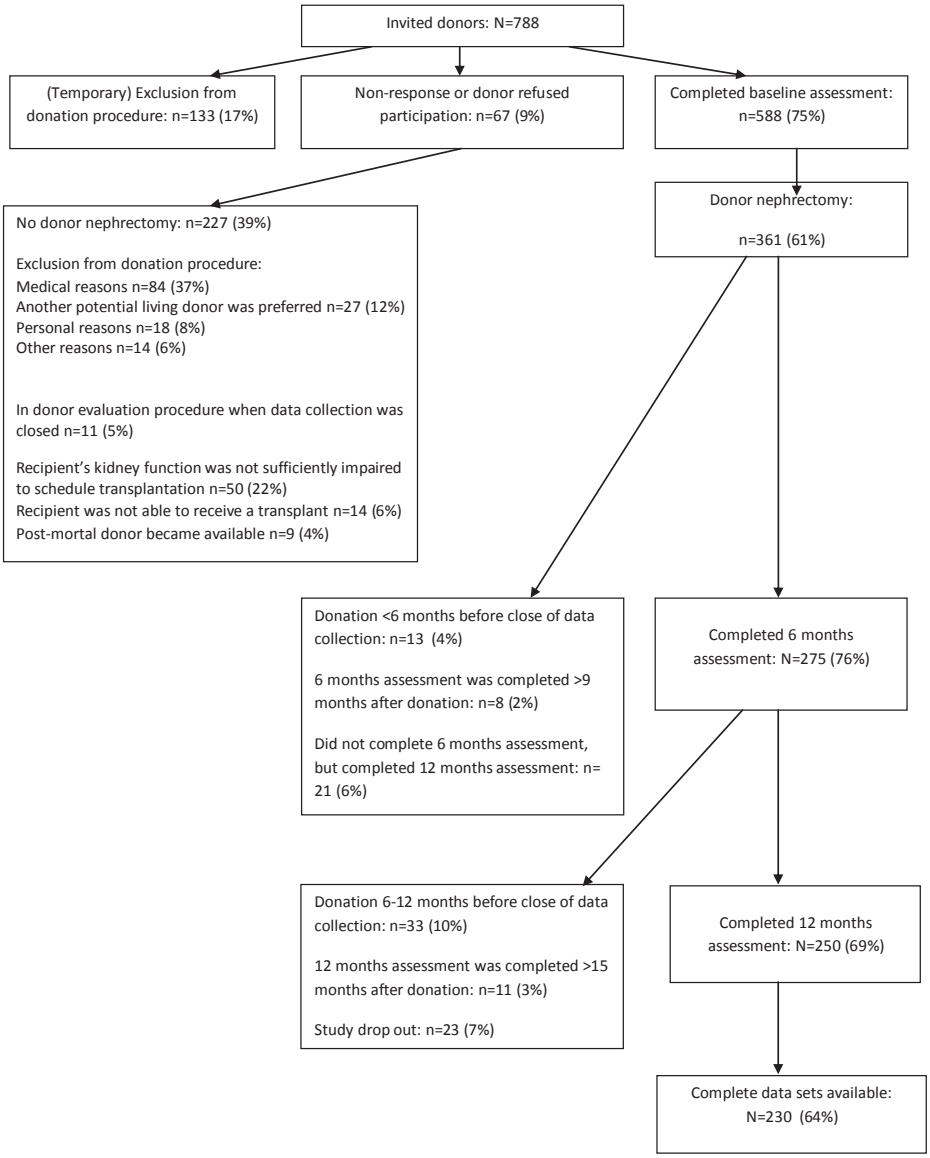


Figure 1. Study Flow Chart

Risk estimations by transplant professionals

Transplant professionals indicated their risk estimation of poorer longer-term donor physical and psychosocial functioning on a 10-point Scale; higher scores represented a higher risk of an unfavorable course. Physical risk estimations were represented in a single item. Psychosocial risk estimations were represented in a summary score based on 1) motivations, expectations, and worries about donation; 2) social support and

recipient-related factors; and 3) past and 4) current psychological functioning (Figure 2). Because risk estimations were not always completed by all four disciplines, an average risk estimation per donor was calculated; in secondary analyses, risk estimations of specific disciplines were explored (estimations of psychologists were excluded because of the small sample size).

Transplant Professionals Questionnaire: Risk estimation of potential kidney donors

I Physical functioning

Current physical functioning:

very poor ——— **very good**

II Motivation and expectations

		Not at all	A little	Somewhat	Strongly	Unknown
1.	The donation is a well-considered choice.	1	2	3	4	❑
2.	The donor expects that					
	… his/her quality of life will improve after the donation.	1	2	3	4	❑
	… the recipient's quality of life will improve after the donation.	1	2	3	4	❑
	… the relationship with the recipient will improve after the donation	1	2	3	4	❑
3.	The donor's expectations about the donation are realistic.	1	2	3	4	❑
4.	The donor is worried about the donation.	1	2	3	4	❑

In light of the motivation and expectations, how high do you estimate the risk of an unfavorable course after the donation?

no risk ——— **very high risk**

III Social environment

		Not at all	A little	Somewhat	Strongly	Unknown
1.	The donor's loved ones are positive about the donation.	1	2	3	4	❑
2.	If problems arise in connection with the donation, there are enough people to whom the donor could turn for help.	1	2	3	4	❑
3.	The donor indicates that he/she has a good relationship with the recipient *(if applicable)*.	1	2	3	4	❑
4.	The donor indicates that he/she can communicate well with the recipient about the donation *(if applicable)*.	1	2	3	4	❑

In light of the social factors, how high do you estimate the risk of an unfavorable course after the donation?

no risk ——— **very high risk**

IV Emotional symptoms – present

	Not at all	A little	Somewhat	Strongly	Unknown
To what extent does the donor currently experience emotional difficulties, such as anxiety or depressed mood?	1	2	3	4	❑

In light of current emotional difficulties, how high do you estimate the risk of an unfavorable course after the donation?

no risk ——— **very high risk**

Figure 2. Transplant professionals' risk estimation questionnaire of poorer longer-term donor functioning

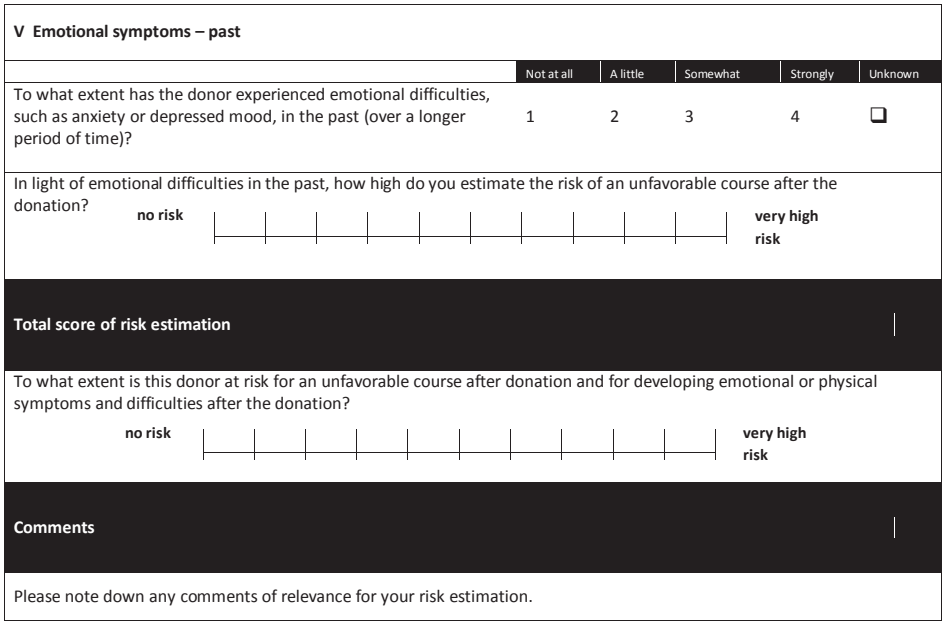


Figure 2. Transplant professionals' risk estimation questionnaire of poorer longer-term donor functioning

Pre-donation donor measures

Donation decision-making

Donation decision-making was assessed by the Donation Cognition Instrument (DCI) (7) and the Living Donation Expectancies Questionnaire (LDEQ) (24).

The DCI consists of two parts: Motivation and Expectations (DCI-ME; 22 items) and Worries (DCI-W; 9 items). The DCI-ME assesses donor motivations and expectations, such as Donor Benefits ('I expect my own quality of life to improve as a result of the donation'); Recipient Benefits ('I wish to donate in order to improve the quality of life of the recipient'); Gratitude ('I expect the recipient to be very grateful for the donation'); and Idealistic Incentives ('I wish to make a contribution to a better world') on a 5-point scale. The DCI-W concerns worries about donation (e.g., 'I am worried about the operation'), measured on a 4-point scale.

The LDEQ examines expectancies regarding donor's personal well-being (42 items), starting with 'As an organ donor, I expect…', measured on a 5-point scale. Six domains are distinguished: Interpersonal Benefits (e.g., '...to be seen as heroic'); Personal Growth (e.g., '...to feel proud of myself'); Spiritual Benefits (e.g., '...to have a stronger religious faith'); Quid Pro Quo (e.g., '...preferential treatment by the recipient after donation'); Health Consequences (e.g., '...to experience a great deal of pain and discomfort'); and Miscellaneous Consequences (e.g., '...to have more financial problems'). Higher scores represent higher expectancies (24).

Health-related quality of life (HRQoL)

HRQoL: **Physical functioning** was assessed using the RAND Short Form-36 Health Status Inventory (RAND SF36; 25) and the Checklist Individual Strength-Fatigue Scale Short Version (CIS; 26).

The RAND SF36 is a 36-item questionnaire assessing eight HRQoL-dimensions. Four dimensions measure physical health: Physical Functioning, Role Limitations due to Physical Health Problems, Pain, and General Health Perceptions; summarized in the Physical Health Composite Score. The Hays norm-based scoring algorithm was applied, transforming raw scores into T-scores (M=50±10 in the general population). Higher scores represent better HRQoL (25).

The CIS short version (4 items) assesses fatigue (e.g., 'I feel tired'). Higher scores represent more fatigue (26).

HRQoL: **Psychological functioning** was assessed using four subscales of the RAND SF36 : Emotional Well-being, Role Limitations due to Emotional Problems, Social Functioning, and Energy; summarized in the Mental Health Composite Score (25).

Additionally, the NEO Personality Inventory-Revised–Neuroticism scale (eight items) assesses the neuroticism personality characteristic on a 5-point scale ('I can handle myself pretty well in crisis')(27). Higher scores represent higher sensitivity for stressful situations.

HRQoL: **Social-relational functioning** was measured using the Interpersonal Sensitivity Measure (IPSM)(28) and the Inventory for Social Reliance (ISR)(29).

Of the IPSM, the subscales Interpersonal Awareness (7 items; e.g., 'I worry about the effect I have on other people') and Timidity (8 items; e.g., I will do something I do not want to do rather than offend or upset someone') were assessed on a 4-point scale. Higher scores represent greater interpersonal awareness or timidity (28).

Perceived support was assessed using the Perceived Social Support scale (5 items) of the ISR (e.g., 'When I am tense or under pressure, there is somebody to help me'). Scores are rated on a 4-point Likert scale. Higher scores represent lower perceived support (29).

Recipient functioning: Donor perspectives on the donor-recipient relationship quality, current physical and emotional recipient functioning , and the influence of recipient's kidney disease on the donor's life were assessed using 10-point scales (e.g., 'To what extent is your life influenced by the recipients' kidney disease?').

Post-donation outcome measures

Physical and psychological HRQoL six and twelve months post-donation were the outcome measures, assessed by the RAND SF36 Physical and Mental Health Composite Scores (25).

Statistical analyses

First, the association of donor demographic characteristics, pre-, intra- and post-operative donor and recipient health status, transplant professionals' risk estimations, and baseline donor measures with HRQoL at 6 and 12 months post-donation was examined using Pearson correlations. Positive correlations indicate that higher predictor values were related to better post-donation HRQoL. To examine the relative contribution of potential predictors, all variables that showed significant correlations to HRQoL at six or twelve months post-donation were included in hierarchical multiple regression analyses for that outcome. To study the specific role of transplant professionals' judgments of donor risk and donor measures in predicting post-donation HRQoL, pairwise regression analyses were conducted with donor demographic characteristics and pre-, intra- and post-operative donor and recipient health status (Block 1) and either transplant professionals' risk estimations or donor self-report measures (Block 2) as predictor variables of physical or psychological HRQoL 6 or 12 months post-donation. If baseline physical or psychological HRQoL was a significant predictor, subsequent analyses were conducted to examine whether specific HRQoL aspects predicted the outcome. Third, the additional contribution of transplant professionals' risk judgments and donor self-report measures on top of the other category was assessed.

A *p*-value below .05 was considered significant, but trend-significant predictors ($p<.10$) were also reported in the tables. Data were analyzed using IBM SPSS software version 22 (30).

RESULTS

Donor characteristics

Demographic characteristics and pre-, intra- and post-operative health status of 230 included donors are reported in Table 1. There was an almost equal gender representation (59% female), with a mean age of 55.1 (SD=10.7; range 23-76) years, and mostly a secondary level education (62%). The majority (83%) donated directly to a recipient they knew. Donors stayed on average 5 days in the hospital, with 35 donors (15%) experiencing either Grade I (n=19; 8%), Grade II (n=14; 6%) or Grade III-b (n=2; 1%) complications (31). In recipients, 11 (6%) kidneys were rejected and 6 (3%) recipients died after kidney transplantation. There were no major donor complications; none of the donors died or had to receive dialysis treatment during the data collection period.

Table 1. Demographic characteristics and pre-, intra-, and post-operative health status of donors (N=230)

Characteristic	Descriptives
Donor baseline characteristics	
Age Mean ± SD (range) years	55.1 ±10.7 (23-76) years
Gender	
Female	59%
Male	41%
Marital status[a]	
Single	19%
Steady partner	81%
Educational level[b]	
Primary education	5%
Secondary education	62%
Tertiary education (higher vocational/university)	33%
Donation type	
Direct	83%
Kidney exchange procedure	8%
Anonymous	9%
Donor-recipient relationship	
Spouse	30%
Parent	20%
Sibling	18%
Child	3%
Other – related (e.g., uncle)	17%
Other – unrelated (e.g., friend)	3%
Anonymous	9%
Religious affiliation[b]	
Religious	53%
Non-religious	47%
Donor health status	
Surgery type	
Mini-incision donor nephrectomy	15%
Laparoscopy	85%
Hospital stay (days)	4.57 ± 1.6 (range 1-14) days
Donor complications[c]	
No complications	85%
Grade I	8%
Grade II	6%
Grade III a	-
Grade III b	1%
Grade IV a	-

Table 1. Demographic characteristics and pre-, intra-, and post-operative health status of donors (N=230) (continued)

Characteristic	Descriptives
Grade IV b	-
Grade V	-
Recipient complications	
Graft failure	
Yes	6%
No	94%
Patient death	
Yes	3%
No	97%

[a] n=228
[b] n=229
[c] Categorisation according the Clavien-Dindo classification system (Dindo et al. 2004)

Predictors of poorer longer-term HRQoL

Physical HRQoL six and twelve months after donation

Poorer physical HRQoL after donation was related to higher transplant professionals' physical risk judgments as well as multiple donor self-report measures (see Table 2).

Demographic and pre-, intra- and post-operative health status

Demographic characteristics and health status explained only 3% and 6% of variance of physical HRQoL six and twelve months post-donation, respectively, with no individual variables being consistent predictors.

Transplant professionals' risk estimations

A higher transplant professionals' risk estimation of a donor's physical functioning was associated with poorer physical HRQoL at six (β=-.21, p=.01; F(6,170)=1.98, p=.07) and twelve months post-donation (β=-.27, p<.001; F(6,170)=4.05, p=.001), adding 4% and 7% of the explained variance, respectively. Regarding specific disciplines, at six months after donation, higher risk estimations of coordinating nurses (β=-.22, p=.02) and medical social workers (β=-.27, p=.003) predicted worse physical HRQoL, and at twelve months all disciplines (.-20≤β≤=-.31, .04≤p≤.001).

Donor measures

Significant predictors of poorer physical HRQoL six months post-donation were a lower baseline physical HRQoL (β=.44, p<.001) and donor estimations of more recipient limitations in daily life (β=.17, p=.01), adding 33% to the total explained variance F(12,166)=.48, p<.001. For poorer physical HRQoL twelve months post-donation, a lower baseline

Table 2. Correlation and multivariable regression coefficients of the prediction of poorer physical health-related quality of life (physical health composite RAND SF-36) six and twelve months after living kidney donation

Predictors	RAND SF36 Physical health Six months after donation				RAND SF36 Physical health Twelve months after donation			
	Correlational analyses		Regression analyses		Correlational analyses		Regression analyses	
	r	*p*	β	*p*	*r*	*p*	β	*p*
Block 1								
Demographic characteristics								
Gender (0=male, 1=female)	-.10	.15			-.12	.09[‡]		
Age	.05	.46			-.03	.67		
Marital status (0=single, 1=partner)	.14	.038[‡]	.14	.06[‡]	.02	.80	.01	.93
Educational level: (0=no, 1=yes)								
primary education	.00	.99			-.02	.82		
secondary education	-.03	.65			.01	.88		
tertiary education	.03	.63			.00	.96		
Work situation (0= not working, 1=working)	-.10	.16			-.06	.37		
Being religious (0= no, 1=yes)	.09	.22			.00	.95		
History of psychological complaints (0=no,1=yes)	-.07	.33			.02	.80		
Donation Type: (0=no, 1=yes)								
direct	.04	.61			.01	.84		
kidney exchange procedure	-.10	.15			-.09	.22		
anonymous	.06	.36			.07	.29		
Donor-recipient relationship: (0=no, 1=yes)								
spouse	-.07	.32			-.08	.27		
parent-child	-.02	.76			-.07	.29		
child-parent	.01	.85			.07	.29		
sibling	.07	34			.06	.38		
other emotionally related	-.01	.85			.06	.40		
other genetically related	-.03	.68			-.08	.28		
Donor health status								
Donor baseline health status								
Physical comorbidity (0=no, 1=yes)	-.08	.27			-.05	.49		
Body Mass Index	-.09	.20			-.11	.12		
Systolic blood pressure	.08	.23			.13	.07[‡]		
Diastolic blood pressure[1]	.09	.22			.13	.07[‡]		
Donor baseline behavioral factors								
Smoking (0=no, 1=yes)	-.07	.33			.01	.90		
Alcohol use (0=no, 1=yes)	.10	.15			.10	.15		

Table 2. Correlation and multivariable regression coefficients of the prediction of poorer physical health-related quality of life (physical health composite RAND SF-36) six and twelve months after living kidney donation (continued)

Predictors	RAND SF36 Physical health Six months after donation				RAND SF36 Physical health Twelve months after donation			
	Correlational analyses		Regression analyses		Correlational analyses		Regression analyses	
	r	*p*	β	*p*	*r*	*p*	β	*p*
Donor intra- and post-operative characteristics								
Surgery type (0=MIDN, 1=LAP)	.03	.63			.04	.56		
Nephrectomy side (0=left)	-.04	.58			.03	.69		
Hospital stay (days)	.04	.59			.16	.02‡		
Donor complications[2]								
No complications	.01	.87			-.13	.06		
Grade I	.03	.65			-.13	.07		
Grade II	.04	.62			-.18	.01‡		
Grade III	.01	.87			-.13	.06		
Recipient health status								
Recipient baseline health status								
Pretransplant treatment recipient: (0=no, 1=yes)								
Pre-emptive	.05	.52			.00	.96		
Haemodialysis	-.01	.93			.01	.87		
Peritoneal dialysis	-.10	.16			.00	.97		
Transplantation	.07	.31			.05	.53		
Recipient post-transplantation complications								
Graft failure (0=no)	13	.08			.01	.85		
Patient death (0=no)	.08	.27			.03	.71		
Block 2								
Risk estimation transplant professionals (VAS)								
Mean physical risk estimation (all transplant disciplines)	-.21	.005§	-.21	.01§	-.31	<.001¶	-.27	<.001§
Nephrologist	-.05	.71	-.04	.76	.24	.04‡	-.20	.04‡
Coordinating nurse	-.20	.01‡	-.22	.02‡	.26	.001§	-.31	.001§
Medical Social Worker	-.29	.001§	-.27	.003§	.27	.002§	-.25	.01§
Donor baseline self-report measures: Donor Cognitions								
Donation Cognition Instrument (DCI)								
Donor Benefits	-.08	.26			-.09	.21		
Recipient Benefits[1]	-.01	.87			-.02	.77		
Idealistic Incentives	.11	.11			.05	.44		
Gratitude	.10	.14			.06	.37		
Worries about the donation[1]	-.10	.16			-.14	.054‡		

Table 2. Correlation and multivariable regression coefficients of the prediction of poorer physical health-related quality of life (physical health composite RAND SF-36) six and twelve months after living kidney donation (continued)

Predictors	RAND SF36 Physical health Six months after donation				RAND SF36 Physical health Twelve months after donation			
	Correlational analyses		Regression analyses		Correlational analyses		Regression analyses	
	r	*p*	β	*p*	*r*	*p*	β	*p*
Living Donation Expectancies Questionnaire (LDEQ)								
Interpersonal Benefit	-.01	.92			-.02	.80		
Personal Growth	.07	.34			.05	.52		
Spiritual Benefit	.05	.49			-.02	.82		
Quid Pro Quo	.07	.40			.05	.51		
Health Consequences	-.10	.20			-.11	.16		
Miscellaneous Consequences	-.07	.34			-.05	.51		
Donor baseline self-report measures: Donor HRQoL								
Physical functioning								
Baseline physical HRQoL (RAND SF36 PCS) [1]	.53	<.001¶	.44	<.001¶	.48	<.001¶	.37	<.001§
Subscales physical HRQoL (RAND SF36)								
Physical functioning[1]	.35	<.001¶	.15	.06ŧ	.33	<.001¶	.13	.10
Physical role limitations	.21	.002§	.08	.28	.21	.002§	.08	.29
Pain[1]	.29	<.001¶	.11	.14	.29	<.001¶	.09	.22
General health perceptions	.43	<.001§	.21	.02ŧ	.40	<.001¶	.21	.02ŧ
Checklist Individual Strength (CIS)								
Fatigue[1]	-.39	<.001¶	-.13	.11	-.32	<.001¶	-.09	.31
Psychologial functioning								
RAND Short Form36 Health Status Inventory MCS								
Emotional functioning[1]	.35	<.001¶	.02	.80	.31	<.001¶	.04	.68
NEO Personality Inventory – Revised (NEO PI R)								
Neuroticism	-.24	.001§	-.05	.52	-.32	<.001¶	-.12	.15
Social-relational predictors								
Interpersonal Sensitivity Measure (IPSM)								
Interpersonal awareness	.13	.06ŧ	.04	.63	.21	.002§	.02	.76
Timidity	-.03	.70			.03	.70		
Inventory for Social Reliance (ISR)								
Social support	.05	.51			.02	.79		
Donor estimation of wellbeing recipient before transplantation								
Quality of donor-recipient relationship[1]	.07	.35			.13	.07ŧ		
Physical functioning recipient	.14	.06ŧ			.11	.14		
Emotional functioning recipient	.08	.31			.09	.23		

Table 2. Correlation and multivariable regression coefficients of the prediction of poorer physical health-related quality of life (physical health composite RAND SF-36) six and twelve months after living kidney donation (continued)

Predictors	RAND SF36 Physical health Six months after donation				RAND SF36 Physical health Twelve months after donation			
	Correlational analyses		Regression analyses		Correlational analyses		Regression analyses	
	r	*p*	β	*p*	*r*	*p*	β	*p*
Limitations of recipient in daily life	.16	.03‡	.17	.01‡	.02	.81	.06	.41
Influence of kidney disease of the recipient on donor's life	.17	.02‡	.03	.64	.16	.03‡	.03	.69
Donor feelings of responsibility for wellbeing recipient	.14	.06†			.09	.26		
Donor taking over workload of recipient	.14	.07†			.05	.54		

† $p<.10$, ‡ $p<.05$, § $p<.01$, ¶ $p<.001$. Positive scores indicate that predictors are related to better physical functioning.

LAP: laparoscopic donor nephrectomy, MIDN: mini-incision donor nephrectomy.

[1]Variables that were not normally distributed and were transformed using logarithmic or reflected transformation, [2]Categorisation according the Clavien-Dindo classification system (Dindo et al. 2004)

physical HRQoL (β=.37, $p<.001$) remained a significant predictor, adding a variance of 22%, $F(12,166)=5.38$, $p<.001$. Looking into the specific aspects of physical HRQoL, the general health perceptions subscale was the only significant predictor at both six (β=.21, $p=.02$) and twelve months (β=.19, $p=.03$) after donation.

Psychological HRQoL six and twelve months after donation

Poorer post-donation psychological HRQoL was related to higher transplant professionals' psychological risk estimations as well as various categories in the donor measures (Table 3).

Demographic characteristics and pre-, intra- and post-operative health status

Demographic characteristics and health status explained 21% and 22% of the variance of psychological HRQoL six and twelve months post-donation, respectively. The only consistent predictor was having a child-parent donor-recipient relationship, which was a protective factor for poorer psychological HRQoL twelve months after donation (in transplant professionals model: β=-.23, $p=.002$; in donor measures model: β=-.19, $p=.02$).

Transplant professionals' risk estimations

A higher risk estimation by transplant professionals regarding donor's psychosocial functioning added 2% and 1% of the variance to the prediction of poorer psychological

Table 3. Correlation and multivariable regression coefficients of the prediction of poorer psychological health-related quality of life (mental health composite RAND SF36) six and twelve months after living kidney donation

	RAND SF36 Mental Health Six months after donation				RAND SF36 Mental Health Twelve months after donation			
	Correlational analyses		Regression analyses		Correlational analyses		Regression analyses	
Predictors	***r***	***p***	**β**	***p***	***r***	***p***	**β**	***p***
Block 1								
Demographic characteristics								
Gender (0=male, 1=female)	-.20	.003[§]	-.15	.051	-.16	.02[‡]	-.10	.19
Age	.03	.66			-.04	.52		
Marital status (0=single, 1=partner)	.15	.03[‡]	.16	.045[†]	.08	.26	.09	.27
Educational level: (0=no, 1=yes)								
primary education	-.08	.25			-.05	.50		
secondary education	.04	.58			.00	.97		
tertiary education	.00	.97			.02	.78		
Work situation (0= not working, 1=working)	-.09	.22			-.03	.63		
Being religious (0=no, 1=yes)	.09	.20			.05	.51		
History of psychological complaints (0=no,1=yes)	-.25	<.001[¶]	-.21	.01[‡]	-.17	.02[‡]	-.14	.07
Donation Type: (0=no, 1=yes)								
direct	.13	.07[†]	.02	.87	.16	.02[‡]	.06	.58
kidney exchange procedure	-.01	.91	.00	.95	-.03	.71	.07	.38
anonymous	-.14	.047[‡]	-.27	.40	-.17	.02[‡]	.20	.55
Donor-recipient relationship: (0=no, 1=yes)								
spouse	-.03	.63	-.04	.64	-.06	.36	.02	.85
parent-child	-.04	.59	.02	.79	-.06	.42	.02	.80
child-parent	.11	.10	.17	.03[‡]	.18	.01[‡]	.22	.004[§]
sibling	.08	.25	.15	.08[†]	.08	.22	.13	.12
other emotionally related	.02	.82	.11	.19	.11	.13	.15	.08[†]
other genetically related	.05	.47	.08	.28	.01	.92	.03	.71
Donor health status								
Donor baseline health status								
Physical comorbidity (0=no, 1=yes)	-.01	.83			-.08	.23		
Body Mass Index	.04	.61			.03	.71		
Systolic blood pressure	.16	.02[‡]	.13	.22	.18	.01[‡]	.10	.32
Diastolic blood pressure[1]	.13	.051[†]	.04	.69	.16	.02[‡]	.09	.40
Donor baseline behavioral factors								
Smoking	-.08	.26			-.04	.54		
Alcohol use	.06	.40			.07	.33		

Table 3. Correlation and multivariable regression coefficients of the prediction of poorer psychological health-related quality of life (mental health composite RAND SF36) six and twelve months after living kidney donation (continued)

	RAND SF36 Mental Health Six months after donation				RAND SF36 Mental Health Twelve months after donation			
	Correlational analyses		Regression analyses		Correlational analyses		Regression analyses	
Predictors	***r***	***p***	**β**	***p***	***r***	***p***	**β**	***p***
Donor intra- and post-operative characteristics								
Surgery type (0=MIDN, 1=LAP)	.06	.38			.09	.20		
Nephrectomy side (0=left)	.04	.55			.06	.41		
Hospital stay (days)	.23	.001§	-.14	.07	.14	.052ǂ	.09	.26
Donor complications[2]								
No complications	.07	34			.08	.23		
Grade I	.08	.23	.04	.80	.05	.48	.27	.11
Grade II	.13	.06ǂ	.32	.09	.12	.08ǂ	.27	.16
Grade III	.08	.27	.17	.49	.09	.19	.09	.70
Recipient health status								
Recipient baseline health status								
Pretransplant treatment recipient: (0=no,1=yes)								
Pre-emptive	-.02	.75			-.01	.86		
Haemodialysis	.01	.93			.02	.74		
Peritoneal dialysis	.01	.93			-.07	.32		
Previous transplantation	.05	.54			.12	.11		
Recipient post-transplantation complications								
Graft failure (0=no)	.01	.85			.02	.79		
Patient death (0=no)	.04	.55			.05	.51		
Block 2								
Risk estimation transplant professionals (VAS)								
Mean psychosocial risk estimation (all transplant disciplines)	-.27	<.001¶	-.15	.053ǂ	-.23	.001§	-.17	.03ǂ
Nephrologist	-.29	.01ǂ	-.17	.25	-.28	.02ǂ	-.17	.25
Coordinating nurse	-.25	.001§	-.05	.61ǂ	-.20	.01ǂ	-.17	.11
Medical Social Worker	-.26	.002§	-.21	.02ǂ	-.20	.03ǂ	-.20	.03ǂ
Donor baseline self-report measures: Donor Cognitions								
Donation Cognition Instrument (DCI)								
Donor Benefits	-.13	.07ǂ			-.13	.07ǂ		
Recipient Benefits[1]	.11	.11			.11	.10		
Idealistic motivations	.16	.02ǂ	.12	.14ǂ	.03	.70	-.04	.62
Gratitude	.16	.02ǂ	.02	.79	.14	.04ǂ	.04	.62
Worries about the donation[1]	-.18	.01ǂ	-.08	.40	-.25	<.001¶	.00	.99

Table 3. Correlation and multivariable regression coefficients of the prediction of poorer psychological health-related quality of life (mental health composite RAND SF36) six and twelve months after living kidney donation (continued)

	RAND SF36 Mental Health Six months after donation				RAND SF36 Mental Health Twelve months after donation			
	Correlational analyses		Regression analyses		Correlational analyses		Regression analyses	
Predictors	***r***	***p***	**β**	***p***	***r***	***p***	**β**	***p***
Living Donation Expectancies Questionnaire (LDEQ)								
Interpersonal Benefit	-.06	.46			-.09	.24		
Personal Growth	-.05	.51			-.05	.53		
Spiritual Benefit	.01	.86			-.04	.62		
Quid Pro Quo	.03	.69			.04	.63		
Health Consequences	-.19	.01‡	.14	.52	-.20	.01‡	.22	.31
Miscellaneous Consequences	-.18	.02‡	.13	.53	-.20	.01‡	-.17	.40
Donor baseline self-report measures: Donor HRQoL								
Physical functioning								
RAND Short Form36 Health Status Inventory PCS								
Baseline physical functioning[1]	.40	<.001¶	.13	.15	.38	<.001¶	.14	.14
Checklist Individual Strength (CIS)								
Fatigue[1]	-.44	<.001¶	-.14	.14	-.39	<.001¶	-.05	.64
Psychological functioning								
Baseline mental HRQoL (RAND SF36) [1]	.53	<.001¶	.26	.02‡	.55	<.001¶	.31	.01‡
Subscales mental HRQoL (RAND SF36)								
Emotional wellbeing	.51	<.001¶	.31	.004‡	.51	<.001¶	.30	.01‡
Emotional role limitations	.21	.002§	.03	.69	.20	.003§	.09	.26
Vitality	.46	<.001¶	.08	.46	.49	<.001¶	.11	.30
Social functioning[1]	.34	<.001¶	.00	.98	.37	<.001¶	.07	.49
NEO Personality Inventory – Revised (NEO PI R)								
Neuroticism	.32	<.001¶	.06	.55	.37	<.001¶	.09	.37
Social-relational predictors								
Interpersonal Sensitivity Measure (IPSM)								
Interpersonal awareness	.28	<.001¶	.04	.73	.30	<.001¶	.06	.58
Timidity	.13	.07†	.00	.99	.16	.02‡	.01	.95
Inventory for Social Reliance (ISR)								
Social support	.06	.42	.10	.26	.20	.004§	.04	.66

Table 3. Correlation and multivariable regression coefficients of the prediction of poorer psychological health-related quality of life (mental health composite RAND SF36) six and twelve months after living kidney donation (continued)

	RAND SF36 Mental Health Six months after donation				RAND SF36 Mental Health Twelve months after donation			
	Correlational analyses		Regression analyses		Correlational analyses		Regression analyses	
Predictors	***r***	***p***	**β**	***p***	***r***	***p***	**β**	***p***
Donor estimation of wellbeing recipient before transplantation								
Quality of donor-recipient relationship[1]	.10	.18			.12	.10		
Physical functioning recipient	.14	.07[†]	.10	.19	.16	.03[‡]	.14	.06[†]
Emotional functioning recipient	.02	.79			.09	.26		
Limitations of recipient in daily life	.01	.95			.06	.46		
Influence of kidney disease of the recipient on donor's life	.17	.02[‡]	.03	.71	.22	.003[§]	.10	.29
Donor feelings of responsibility for wellbeing recipient	.10	.17	.06	.54	.17	.03[‡]	.04	.69
Donor taking over workload of recipient	.01	.94			.09	.21		

[†] $p<.10$, [‡] $p<.05$, [§] $p<.01$, [¶] $p<.001$. Positive scores indicate that predictors are related to a better mental HRQoL
LAP: laparoscopic donor nephrectomy, MIDN: mini-incision donor nephrectomy.
[1]Variables that were not normally distributed and were transformed using logarithmic or reflected transformation
[2]Categorisation according the Clavien-Dindo classification system (Dindo et al. 2004)

HRQoL at six (β=-.15, $p=.053$; $F(18,160)=2.71$, $p<.001$) and twelve months after donation, (β=.17, $p=.03$; $F(18,160)=2.61$, $p=.001$). Higher risk estimations of medical social workers (6 months: β=-.21, $p=.02$; 12 months: β=-.20, $p=.03$) significantly predicted worse psychological HRQoL after donation.

Donor measures

Of donor measures, poorer baseline psychological HRQoL was the only significant predictor of poorer psychological HRQoL six (β=.26, $p=.02$; $F(32,120)=3.15$, $p<.001$) and twelve months post-donation (β=.31, $p=.01$; $F(32,120)=3.08$, $p<.001$), adding 25 and 23% explained variance. Looking into the specific aspects of psychological HRQoL, poorer emotional well-being was the only significant predictor at both six (β=.31, $p=.004$) and twelve (β=.30, $p=.01$) months post-donation.

Relative contribution of transplant professionals' risk estimations and donor measures

Both transplant professionals' risk estimations and donor measures added significant variance to the prediction of physical and psychological HRQoL on top of demographic variables and health status. The additional value of transplant professionals' risk esti-

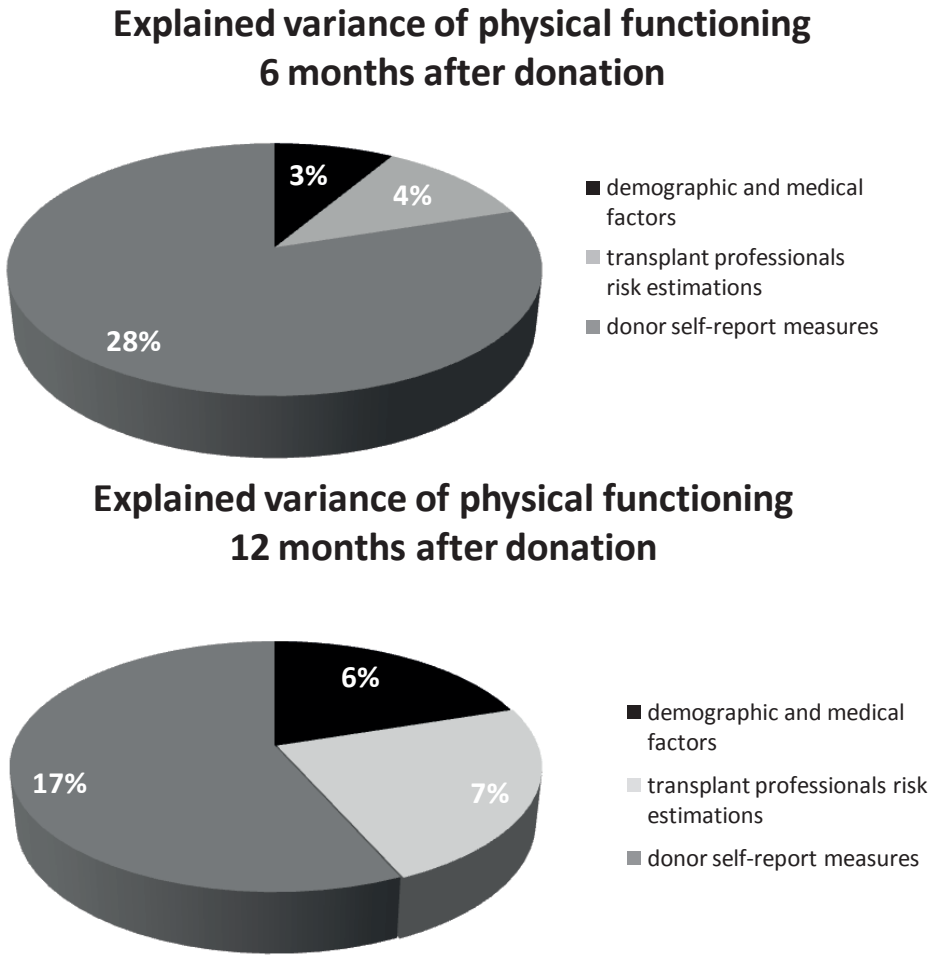


Figure 3. Relative contribution of donor demographic/medical factors, transplant professionals' risk estimations, and donor self-report measures on the explained variance of physical functioning 6 and 12 months after donation

mations on top of donor measures was limited in predicting both physical (0-2%) and psychological HRQoL (0-1%), while using donor measures added 17-28% of explained variance in physical and 23% in psychological HRQoL on top of transplant professionals' risk estimations (see Figure 3 and Figure 4).

To rule out the influence of potential bias by specific drop-out, analyses of donors with complete assessments were repeated in donors completing only the six (n=275) or twelve (n=250) months assessment. This led to very similar results (correlations>.97 with predicted values).

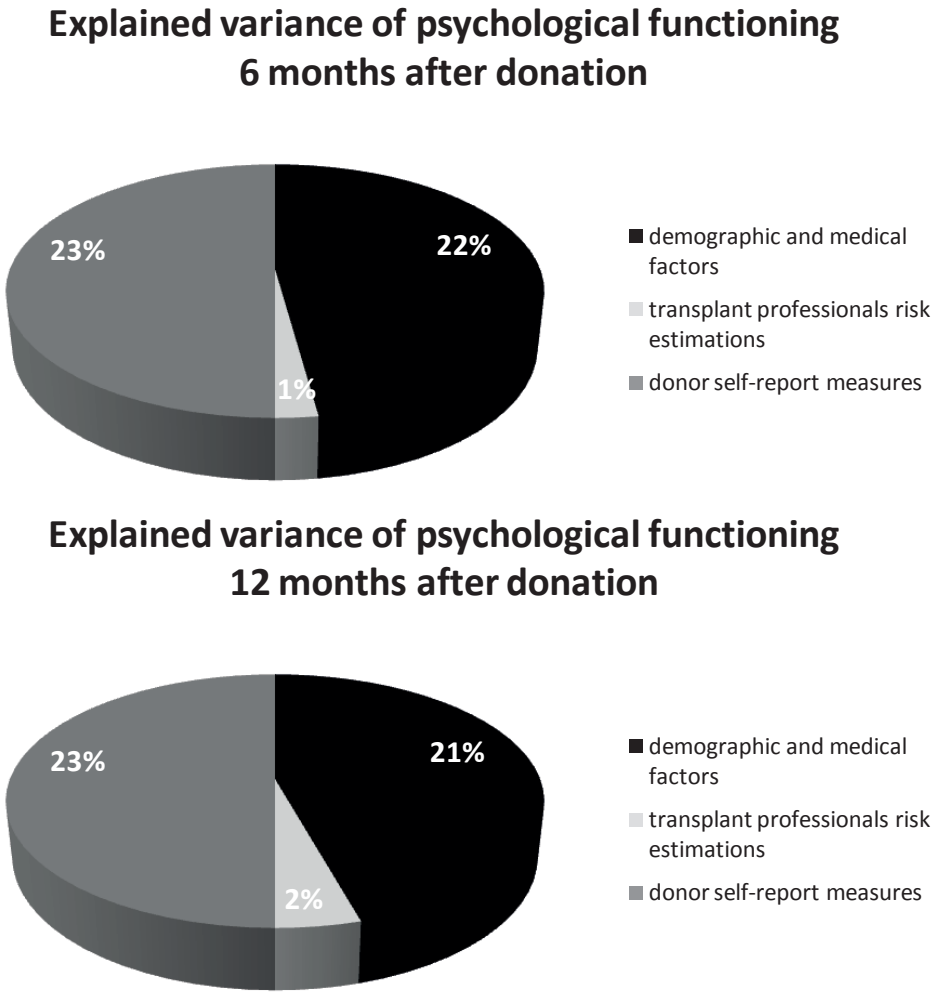


Figure 4. Relative contribution of donor demographic/medical factors, transplant professionals' risk estimations, and donor self-report measures on the explained variance of psychological functioning 6 and 12 months after donation

DISCUSSION

Currently, the psychosocial donor evaluation is mainly based on clinical judgments of transplant professionals. An evidence-based evaluation would enable transparent eligibility decisions and interventions for donors with a high-risk profile. This study examined the effectiveness of the current psychosocial donor evaluation by transplant professionals, and the potential improvement of the evaluation using donor self-report measures. Results showed that both transplant professionals' risk judgments and donor

self-report measures predicted longer-term donor HRQoL, which endorses the quality of the professionals' evaluation. Importantly, using donor self-report measures improved the predictive value of professionals' risk assessments.

The finding that donor self-report measures optimize transplant professionals' eligibility screening, confirms previous research indicating that patient-reported outcomes (PROs) can improve the quality of clinical decision-making and efficiency of consultations (32, 33). In addition, self-report questionnaires could provide (potential) donors insight into donation decision-making, and evaluate the donation experience. Nevertheless, donor self-report measures could not replace professionals' risk assessments because of the potential influence of socially desirable responses due to an often strong desire for donation.

In line with previous studies, baseline HRQoL levels were shown to best predict longer-term HRQoL in the current study (34, 35). Possibly, the other variables (e.g., pre-donation cognitions) contribute indirectly to post-donation HRQoL through their association with baseline HRQoL. Impaired longer-term donor physical functioning was predicted by higher risk estimations of all transplant professionals, while only medical social workers predicted longer-term psychological functioning. This could indicate that donors prefer to share psychosocial problems with social workers, but it could also reveal potential time constraints to discuss psychosocial issues during consultations.

Based on the current study, evidence-based criteria could be added to donor screening guidelines. In order to examine the potential role of an encompassing number of PROs, a large amount of questionnaires was used in the current study. However, based on the results, in clinical practice screening could be conducted in a stepwise fashion, using a short screening questionnaire to obtain an indication of HRQoL before starting the donor evaluation (e.g., the RAND SF36, which takes about 10 minutes to complete). These results could be integrated into eligibility screening consultations with transplant professionals, to increase awareness or clarification of possible problems in potential donors. If a risk profile (lowered HRQoL) is found, additional assessments could identify specific donation-related problems to offer tailored interventions.

This study provides good indications of the most important factors in donor eligibility screening. Nonetheless, the results may have been influenced by a number of factors. The 75% response rate might limit generalizability of the findings to the total donor population. However, the selection bias is probably limited because the most prominent reason for non-participation was exclusion from the donation procedure by professionals (17%). Also, the screening questionnaire was completed at the beginning of the donor evaluation, in order to prevent the exclusion of donors later on in the trajectory, and provide support to high-risk donors. At this time, the motivation to donate dominates and probably fewer worries about the surgery are experienced in comparison with the weeks before surgery. Consequently, an additional donor self-report screening could

be useful when surgery is planned, to provide interventions for donors experiencing distress. Also, there was a large variability in time (*M*= 7 months) between screening and donation, which could be representative for the kidney donor population.

The Dutch healthcare setting of kidney donors cannot automatically be generalized to other healthcare settings in terms of access to care and regulations for health insurance, which are well-organized and available to all inhabitants. Future studies should examine this generalization of findings. Finally, although we aimed to include an encompassing set of predictors, there might be other predictors of longer-term HRQoL of kidney donors. Future research should include these potential predictors (e.g., ambivalence and coercion) and validate those that were identified in the current study (36). Lastly, donor HRQoL could not always be predicted at baseline (e.g., in the case of other life events). Therefore, flexibility in donor follow-up needs to be warranted.

In conclusion, the psychosocial donor evaluation conducted by professionals is effective in predicting longer-term donor HRQoL. Donor self-report measures, with particularly poorer baseline physical and psychological functioning, could optimize the psychosocial evaluation of professionals. This can improve reliable donor eligibility decisions and tailored interventions for high-risk donors.

REFERENCES

1. Chen KH, Yeh LC, Huang HL, et al. Factors Determining Physical and Mental Quality of Life of Living Kidney Donors in Taiwan. Transplant Proc. 2016; 48: 745-748.
2. Clemens KK, Thiessen-Philbrook H, Parikh CR, et al. Psychosocial health of living kidney donors: a systematic review. Am J Transplant. 2006; 6: 2965-2977.
3. Fallahzadeh MK, Jafari L, Roozbeh J, et al. Comparison of health status and quality of life of related versus paid unrelated living kidney donors. Am J Transplant. 2013; 13: 3210-3214.
4. Gross CR, Messersmith EE, Hong BA, et al. Health-related quality of life in kidney donors from the last five decades: results from the RELIVE study. Am J Transplant. 2013; 13: 2924-2934.
5. Mjoen G, Stavem K, Westlie L, et al. Quality of life in kidney donors. Am J Transplant. 2011; 11: 1315-1319.
6. Wirken L, van Middendorp H, Hooghof CW, et al. The Course and Predictors of Health-Related Quality of Life in Living Kidney Donors: A Systematic Review and Meta-Analysis. Am J Transplant. 2015; 15: 3041-3054.
7. Wirken L, van Middendorp H, Hooghof CW, et al. Pre-donation cognitions of potential living organ donors: the development of the Donation Cognition Instrument in potential kidney donors. Nephrol Dial Transplant. 2017; 32: 573-580.
8. Giessing M, Reuter S, Schonberger B, et al. Quality of life of living kidney donors in Germany: a survey with the Validated Short Form-36 and Giessen Subjective Complaints List-24 questionnaires. Transplantation. 2004; 78: 864-872.
9. Jacobs C, Johnson E, Anderson K, Gillingham K, Matas A. Kidney transplants from living donors: how donation affects family dynamics. Adv Ren Replace Ther. 1998; 5: 89-97.
10. Timmerman L, Laging M, Timman R, et al. The impact of the donors' and recipients' medical complications on living kidney donors' mental health. Transpl Int. 2016; 29: 589-602.
11. Andersen MH, Bruserud F, Mathisen L, Wahl AK, Hanestad BR, Fosse E. Follow-up interviews of 12 living kidney donors one yr after open donor nephrectomy. Clin Transplant. 2007; 21: 702-709.
12. Rodrigue JR, Paek M, Whiting J, et al. Trajectories of perceived benefits in living kidney donors: association with donor characteristics and recipient outcomes. Transplantation. 2014; 97: 762-768.
13. Reimer J, Rensing A, Haasen C, Philipp T, Pietruck F, Franke GH. The impact of living-related kidney transplantation on the donor's life. Transplantation. 2006; 81: 1268-1273.
14. Matas AJ, Hays RE, Ibrahim HN. Long-Term Non-End-Stage Renal Disease Risks After Living Kidney Donation. Am J Transplant. 2016: 893-900.
15. Duerinckx N, Timmerman L, Van Gogh J, et al. Predonation psychosocial evaluation of living kidney and liver donor candidates: a systematic literature review. Transpl Int. 2014; 27: 2-18.
16. Iacoviello BM, Shenoy A, Hunt J, Filipovic-Jewell Z, Haydel B, LaPointe Rudow D. A Prospective Study of the Reliability and Validity of the Live Donor Assessment Tool. Psychosomatics. 2017; 58: 519-526.
17. Bahler CD, Sundaram CP. Quality of life following laparoscopic living-donor nephrectomy. JSLS. 2013; 17: 273-278.
18. Chien CH, Wang HH, Chiang YJ, Chu SH, Liu HE, Liu KL. Quality of life after laparoscopic donor nephrectomy. Transplant Proc. 2010; 42: 696-968.
19. de Groot IB, Stiggelbout AM, van der Boog PJ, Baranski AG, Marang-van de Mheen PJ, group PA-s. Reduced quality of life in living kidney donors: association with fatigue, societal participation and pre-donation variables. Transpl Int. 2012; 25: 967-975.

20. Jacobs CL, Gross CR, Messersmith EE, et al. Emotional and Financial Experiences of Kidney Donors over the Past 50 Years: The RELIVE Study. Clin J Am Soc Nephrol. 2015; 10: 2221-2231.
21. Timmerman L, Timman R, Laging M, et al. Predicting mental health after living kidney donation: The importance of psychological factors. Br J Health Psychol. 2016; 21: 533-554.
22. Lennerling A, Loven C, Dor FJ, et al. Living organ donation practices in Europe - results from an online survey. Transpl Int. 2013; 26: 145-153.
23. Dutch Transplant Foundation. 2016.
24. Rodrigue JR, Guenther R, Kaplan B, Mandelbrot DA, Pavlakis M, Howard RJ. Measuring the expectations of kidney donors: initial psychometric properties of the Living Donation Expectancies Questionnaire. Transplantation. 2008; 85: 1230-1234.
25. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-Item Health Survey 1.0. Health Econ. 1993; 2: 217-227.
26. Vercoulen JH, Swanink CM, Fennis JF, et al. Dimensional assessment of chronic fatigue syndrome. J Psychosom Res. 1994; 38: 383-392.
27. Costa PT, Jr., & McCrae, R. R. The NEO Personality Inventory manual. Odessa: Psychological Assessment Resources; 1985.
28. Boyce P, Parker G. Development of a scale to measure interpersonal sensitivity. Aust N Z J Psychiatry. 1989; 23: 341-351.
29. Dam-Baggen RKF. De Inventarisatielijst Sociale Betrokkenheid (ISB): een zelfbeoordelingslijst om sociale steun te meten (Inventory for social reliance (ISR): a self-report inventory for the measurement of social support). Gedragstherapie. 1992; 25: 27-46.
30. IBM SPSS Statistics. IBM Corp. Released 2011. In: Windows ISSf, editor. Version 20.0 ed. Armonk, New York: IBM Corp.
31. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004; 240: 205-213.
32. McCollum L, Pincus T. A biopsychosocial model to complement a biomedical model: patient questionnaire data and socioeconomic status usually are more significant than laboratory tests and imaging studies in prognosis of rheumatoid arthritis. Rheum Dis Clin North Am. 2009; 35: 699-712.
33. Palmer D, El Gaafary M, El Miedany Y. Improving patient care: measurement of outcome in rheumatoid arthritis. Br J Nurs. 2007; 16: 1010-1015.
34. Dunn WR, Wolf BR, Harrell FE, Jr., et al. Baseline predictors of health-related quality of life after anterior cruciate ligament reconstruction: a longitudinal analysis of a multicenter cohort at two and six years. J Bone Joint Surg Am. 2015; 97: 551-557.
35. Jarvholm K, Karlsson J, Olbers T, et al. Characteristics of adolescents with poor mental health after bariatric surgery. Surg Obes Relat Dis. 2016; 12: 882-890.
36. Dew MA, DiMartini AF, DeVito Dabbs AJ, et al. Preventive intervention for living donor psychosocial outcomes: feasibility and efficacy in a randomized controlled trial. Am J Transplant. 2013; 13: 2672-2684.

Chapter 6

Development and feasibility of a guided and tailored internet-based cognitive-behavioral intervention for kidney donors.

Wirken L, van Middendorp H, Hooghof CW, Bremer TE, Hopman SPF, van der Pant KAMI, Hoitsma AJ, Hilbrands LB, Evers AWM

In revision.

ABSTRACT

Background: A subgroup of the kidney donor population experiences adjustment problems during or after the donation procedure (e.g., anxiety or fatigue). There is a need for evidence-based interventions that decrease donation-related difficulties. In the current study, a guided and tailored Internet-based Cognitive-Behavioral Therapy (ICBT) intervention for donors was developed and the feasibility and perceived effectiveness were evaluated.

Methods: Focus group interviews with donors and healthcare professionals were conducted to identify intervention themes and to map attitudes towards internet-based interventions. Donation-related treatment modules, assignments, and psycho-education were integrated within an existing disease-generic ICBT intervention. Eight (potential) donors with a risk profile (i.e., impaired mental HRQoL) received and evaluated the intervention.

Results: Different intervention themes were derived from the focus group interviews (e.g., physical limitations, and donation-specific emotional and social-relational problems). Participants were satisfied about the intervention content and the therapeutic relationship, and indicated an improvement on domains of their treatment goals.

Conclusions: This study showed positive evaluations concerning both feasibility and perceived effectiveness of the tailored ICBT intervention in (potential) kidney donors, in line with previous studies using comparable ICBT treatment protocols in other populations. Future research should examine the possibilities of integrating the intervention into psychosocial care for kidney donors.

INTRODUCTION

Because of the increase in the number of living donor kidney transplantations during the past years, research on the need for psychosocial care of kidney donors has expanded. An important aspect of these studies is the identification of characteristics of donors who might benefit from psychosocial interventions before or following donation (1-3). In order to apply for living kidney donation, potential donors need to have a good physical and mental health-related quality of life (HRQoL). Previous research has shown that in general, the HRQoL of actual donors is equal to or above that of the general population, and either stays stable or returns to baseline within six to twelve months post-donation (4-6). However, it has also been shown that a proportion of donors (up to 35%) develops adjustment problems during or after the donation procedure, such as anxiety, fatigue, or pain (5, 7, 8).

Within the current healthcare protocols for (potential) living kidney donors, psychosocial care before and after donation is not systematically embedded. Screening of donor eligibility is mainly based on medical criteria and although the need for psychosocial screening is increasingly recognized (9, 10), this is currently not conducted in an evidence-based manner. Also, although there generally is a medical donor follow-up up to 12 months post-donation, both short-term (up to 6 months after donation) and longer-term (e.g., 12 months or longer after donation) psychosocial donor follow-up is often lacking, even though recent guidelines do recommend this (11). Reasons for this include a scarcity of large prospective studies showing pre-donation predictive factors of impaired HRQoL after donation. The few large prospective studies conducted have mainly shown worse pre-donation mental and physical functioning to be predictive of worse HRQoL-outcomes after donation, next to a number of individual risk and resilience factors which might be used to tailor treatment to the specific profile of the individual donor (3, 5, 6, 12). Tailored interventions, specified to the individual characteristics, preferences, and needs of (potential) donors to improve health or change behavior, are scarce. However, because of the differences in donor characteristics and the type of difficulties before or after donation, such as pre-donation worries or post-donation fatigue symptoms, tailored interventions could be useful for donors at risk for longer-term adjustment problems.

Currently, a small number of interventions for (potential) donors are available, which mostly focus on donor recruitment (13). Further, one intervention is available for potential donors who are scheduled for surgery, using pre-donation motivational interviewing in two telephonic sessions to reduce ambivalence towards donation. Results of the RCT on the effectiveness of this intervention were positive, with a decline in ambivalence before donation in the intervention group, and better physical functioning, shorter recovery times, less anxiety, and fewer unexpected donation-related family problems

three months after donation (14). To our knowledge, no psychosocial interventions for (potential) donors with a risk profile for a variety of donation-related difficulties are available. Therefore, there is a need for evidence-based interventions that focus on decreasing difficulties in potential donors during the donor screening procedure or negative consequences after donation (15, 16).

Cognitive-behavioral therapy is a worldwide used evidence-based psychological intervention, which is used to treat mental health conditions, focusing on the replacement of maladaptive cognitions and coping strategies by more positive cognitions and behaviors. To this aim, different techniques are used, including the training of problem-solving skills, relaxation training, stress management, and cognitive restructuring, which entails changing unhelpful cognitions into helpful ones (17, 18). Previous research showed that cognitive-behavioral therapy that is provided via the internet (Internet-based Cognitive-Behavioral Therapy or ICBT) could be as effective as face-to-face treatments in the improvement of physical and psychological functioning in patients with mental and physical health problems (19-21). One component that has proven to be associated with the effectiveness of ICBT is online guidance by a therapist during the treatment, for example by means of e-mail messages providing motivating remarks and feedback on assignments (22-24). Additionally, there is increasing evidence that the tailoring of interventions to the specific risk and resilience factors of individuals increases the effectiveness of (I)CBT (25-27). The advantages of cognitive-behavioral interventions using the internet in comparison to face-to-face treatment in the hospital include that individuals can follow the treatment from their own homes, which improves the application of learned techniques directly in their own environment, and that treatment can be followed in their own time, improving flexibility and preventing travel costs and waiting times (28).

In conclusion, current psychosocial care for (potential) living kidney donors at risk for long-term adjustment problems is limited and not evidence-based. Guided and tailored ICBT could be a valuable addition to current psychosocial care for living donors, in providing pre-donation support or short-term or longer-term psychosocial follow-up for donors with a risk profile. The current study describes the development of a guided and tailored ICBT intervention for (potential) donors, and examines the satisfaction with and feasibility of this intervention in a pilot study in a small group of (potential) donors.

MATERIALS AND METHODS

Development of the guided and tailored ICBT intervention for donors

Three steps have been taken to develop the guided and tailored ICBT intervention for (potential) kidney donors and test it's feasibility.

1. Focus group interviews

Three focus group interviews were conducted with donors from two transplantation centers from different parts of the Netherlands, in order to provide a good representation of the Dutch donor population in terms of socio-demographic characteristics and cultural background (Radboudumc Nijmegen and Academic Medical Center Amsterdam). Also, one focus group interview with transplant professionals was conducted (nephrologists, nurses, and medical social workers) in one transplantation center (Radboudumc). The aim of these focus groups was to identify possible themes that would be considered relevant by (potential) donors and transplant professionals to be included in a donor-specific intervention, and to map general attitudes towards internet-based interventions. A health psychologist with background experience in group therapy guided all focus group interviews as a mediator and another psychologist was present as an observer. Focus group interviews were audio and video recorded. Participants (potential donors as well as transplant professionals) signed informed consent at the start of the interviews. The medical ethics committee of the Radboudumc Nijmegen approved the study (NL.50145.091.14).

The focus group interviews started with questions about the possible physical limitations and psychological consequences before and following donation, the influence of the donation on social relationships and daily functioning, and the ways by which donors handled potential problems in their functioning. Also, questions were asked about the perceived potential need for additional psychosocial care and the themes on which this care should be focused according to both donors and transplant professionals. Further, the attitudes of both groups towards ICBT interventions were explored.

2. Evaluation and adjustment of existing ICBT interventions for patients with somatic conditions

Before the start of the current study, our research group developed a generic guided and tailored ICBT intervention, based on evidence-based face-to-face CBT for patients with chronic somatic conditions. The effectiveness of this ICBT intervention was demonstrated in a randomized controlled trial in different patient populations (27, 29). Based on the themes identified in the focus group study and previous (intervention) studies in living kidney donors, the existing generic ICBT intervention was adjusted to incorporate specific donation-related treatment modules, exercises, and psycho-education, resulting in the ICBT intervention for donors. This ICBT intervention is a therapist guided intervention, tailored to the individual treatment goals of donors.

3. Feasibility testing of the ICBT intervention

Research procedure feasibility study

Individuals who donated a kidney for transplantation or were registered as a (potential) donor from November 2014 to August 2015 were invited to participate in the study by means of an information letter. When (potential) donors were interested in participating in the study, a two-step procedure was followed. After signing informed consent, they were asked to fill in several questionnaires to provide a risk categorization based on their current mental HRQoL or psychological distress (see next paragraph). Participants with a psychological risk profile were invited to participate in the pilot intervention study, in which they received the ICBT intervention. After finishing the intervention, participants received a questionnaire to evaluate the ICBT intervention. Next to these subjective donor evaluations, the intervention was evaluated more objectively with technical usage data on the dedication to the intervention and the intervention duration.

Screening questionnaires

Screening questionnaires were used to make a risk categorization based on current mental HRQoL or psychological distress, assessed with the RAND Short Form-36 Health Status Inventory - Mental Health Subscale (RAND SF36)(30), and the Hospital Anxiety and Depression Scale (HADS)(31). A psychological risk profile was defined as RAND SF36 Mental Health subscale scores ≤ 48 or HADS anxiety or depression scores ≥ 5).

The RAND SF36 is a 36-item questionnaire assessing eight HRQoL-dimensions. Four dimensions measure psychological functioning: Emotional Well-being, Role Limitations due to Emotional Problems, Social Functioning, and Energy. These are summarized in the Mental Health Composite Score, which was used in the screening. Higher scores represent higher mental HRQoL (30).

The HADS consists of 7 items measuring anxiety (e.g., 'I get a sort of frightened feeling as if something awful is about to happen') as well as 7 items on depressive symptoms (e.g., 'I feel as if I am slowed down'). Scores are rated on a 4-point scale; higher scores represent more anxiety or depressive symptoms (31).

Intervention tailoring questionnaires

To tailor the ICBT intervention to individual treatment goals, additional questionnaires were used to identify specific problem areas of functioning, distinguishing Physical functioning (RAND SF36 PCS30), Fatigue (Checklist Individual Strength-Fatigue Scale Short Version; 32), Neuroticism (NEO Personality Inventory- Revised- Neuroticism; 33), Social-relational functioning (Interpersonal Sensitivity Measure (34) and the Inventory for Social Reliance (35)).

ICBT intervention evaluation measures

Satisfaction with the ICBT intervention

The information provision before the intervention, the degree to which expectations of the intervention were met, the general satisfaction with the intervention, the donor beliefs about a sustainable effect of the intervention, and the extent to which donors would recommend the intervention to relatives were evaluated directly after finishing the intervention. Furthermore, the dedication towards the intervention and the effect of the intervention on treatment goals were evaluated. All evaluations were made on a 4-point scale (1=no, 4=certainly). Higher scores represent more satisfaction with the intervention, more active participation in the intervention, and more effect of the intervention on treatment goals.

Feasibility of the ICBT intervention

The comprehensibility and usefulness of the assignments and psycho-educational texts were assessed using a 7-point scale (0=very poor-6=very good).

Therapeutic relationship

The therapeutic relationship during the ICBT intervention was assessed using the Working Alliance Inventory (WAI) and the Internet-Specific Therapeutic Relationship Questionnaire (ITRQ).

The WAI assesses the working alliance concepts of therapeutic relationships, consisting of three subscales, namely agreement on therapy goals, on therapy tasks, and the development of a strong relational bond between patient and therapist, assessed on a 1-5 scale (1=never to 5= always)(36, 37).

The ITRQ measures internet-specific aspects of the therapeutic relationship during internet-based interventions, consisting of two 4-item subscales: Internet-specific time and attention (which assesses time lag aspects of communication and receiving sufficient attention from the ICBT therapist) and Internet-specific reflection and comfort (which comprises the sharing of information with the therapist and home as the treatment environment) on a 1-10 scale (1=totally disagree - 10= totally agree)(38).

Usage of the ICBT intervention

To gain insight into the use of the intervention website with objective parameters, the frequency of logins per donor and the total intervention duration were assessed.

RESULTS

Intervention development

1. Focus group interviews

Participants

Focus group interviews were conducted with 13 donors post-donation, of whom 69% were female and who had a mean age of 58.8 years (age range: 30-74 years). Most donors had donated directly to the person they knew (77%), but also kidney donor exchange (8%) and altruistic (15%) donors were represented. In the focus group interview with transplant professionals, one nephrologist, one coordinating nurse, and three medical social workers participated, with a mean work experience in the field of transplantation of 6.0 years (range 3-13 years) (see Table 1 for participants' characteristics).

Table 1. Demographic characteristics of donors and transplant professionals participating in the focus group interviews and pilot study of the ICBT intervention

Characteristics	Mean ± SD (range) N (%)
Participants of the focus group interviews	
Donor characteristics (N=13)	
Female gender	9 (69%)
Age	58.8 ± 11.5 years (range: 30-74)
Donation type	
Direct	10 (77%)
Kidney exchange	1 (8%)
Altruistic	2 (15%)
Time since donation	2.4 ± 1.7 years (range: 0.6-7.0)
Donation professionals characteristics (N=5)	
Type professional	
Nephrologist	1 (20%)
Donation coordinating nurse	1 (20%)
Medical social worker	3 (60%)
Work experience in transplantation care	6.0 ± 4.2 years (range: 3-13 years)
Participants of pilot study on the ICBT intervention	
(Potential) donor characteristics (N=8)	
Female gender	5 (63%)
Age	58.6 ± 11.4 years (range: 38-74)
Donation type	
Direct	6 (75%)
Kidney exchange	1 (13%)
Altruistic	1 (13%)

Intervention themes

In the focus group interviews, donors and transplant professionals identified a number of themes that were considered to be useful to include in donor interventions. These included high levels of fatigue and related concentration problems, pain, problems with getting back to work, dealing with the simultaneous presence of the donor's own temporary limitations after surgery and limitations for the recipients, worries about the recipient (e.g., graft failure or re-hospitalization), dealing with waiting times for transplantation after being eligible for donation, the influence of donation on family life and relationships, and sharing donation experiences with other (potential) donors. These themes were used for the adjustment of the existing ICBT intervention. Finally, despite overall satisfaction with the consultations with medical social workers during eligibility screening, donors indicated a need to optimize the follow-up contacts after donation, with more attention for psychosocial issues.

2. Feasibility testing of the ICBT intervention

Participants pilot study

Ninety-nine individuals (47 potential donors and 52 donors) were invited to participate in the pilot study. Of these, 14 potential donors (30% response rate) and 24 donors (46% response rate) completed the screening questionnaire, of which 16 donors (42%) had a higher risk profile. Three of these donors indicated that they experienced only minor difficulties and were not interested in the intervention, and five donors did not respond to the invitation for intervention. Two potential donors and six donors received the tailored ICBT intervention to reduce donation-related distress, of whom 5 were female and 3 were male. Age varied from 38 to 74 years, with a mean age of 59±11 years. Of potential donors, one was on the kidney exchange program and one intended to donate directly to the person he/she knew; of the donors, 5 donated directly to the person they knew and one donated anonymously (Table 1).

Procedure of the ICBT intervention

After signing informed consent, participants were invited for a face-to-face appointment with their therapist, to get acquainted and formulate treatment goals based on the screening questionnaire or current causes of distress. The intervention was provided by one therapist with a Master's degree on clinical psychology and a clinical registration as Health Psychologist. The intervention consisted of five different treatment modules with focus on the following items: physical limitations, fatigue, negative mood, social functioning, and donation-related problems in daily life (see Figure 1). After the face-to-face consultation with their therapist, an instruction of the use of the website was provided by telephone by a research assistant. Afterwards, the (potential) donor could log on to the secure website to start with the ICBT intervention that was tailored to

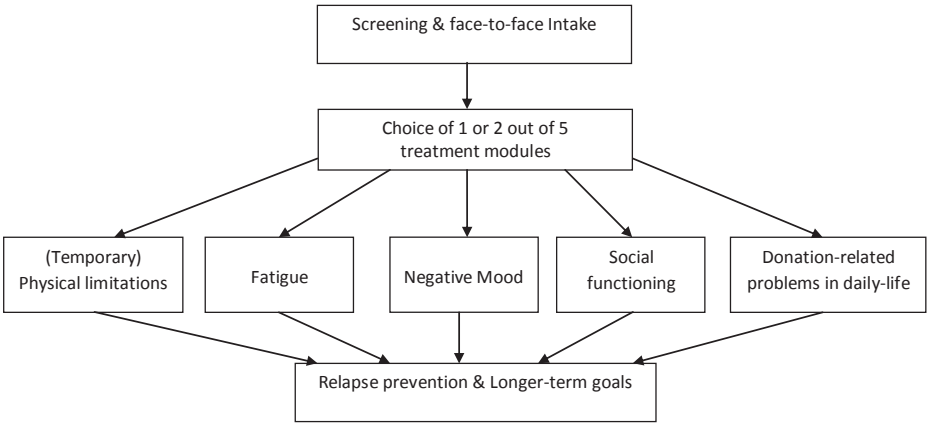


Figure 1. Intervention Procedure

their own treatment goals. Assignments and psycho-educational texts related to the treatment goals were placed on the website by the therapist and completed online by the (potential) donor. The therapist provided personalized feedback on the exercises weekly via a message box and donors could reply to the therapist or ask questions via this message box. After finishing the personalized modules, the treatment was ended with a final treatment module about relapse prevention and the formulation of long-term goals. See Figure 1 for the structure of the intervention.

Within the group of eight participants, all five treatment modules were applied at least once; two donors worked on negative mood and donation-related problems in daily life, two donors on negative mood and fatigue, one donor on physical limitations and social functioning, one donor on fatigue and social functioning, one donor on negative mood, and one donor on fatigue. The intervention had a mean duration of 11.6 weeks (range 3-18 weeks). Two potential donors followed the intervention before donation (time until donation was M=1.5±0.4 months), and six donors after donation (time between donation and intervention was M=6.4±3.6 months).

Evaluation of the intervention

Participants were satisfied with the ICBT intervention (M=7.7, range: 6-8 on a 0-10 scale). On 1-4 scales they reported that the intervention met their expectations (M=3.4), that they had received appropriate information before the start of the treatment (M=4.0), and that they thought that the treatment effect would persist on the longer-term (M=3.4). Most donors would recommend the ICBT intervention to future donors (M=3.6). With regard to the dedication to the treatment, participants reported that they usually conducted the assignments that the therapist sent them (M=3.0), and that they worked on the treatment goals intensively (M=3.3), practicing the assignments and integrating

the learned strategies in daily life (*M*=3.1). Most participants did not have a fixed moment of time to conduct the assignments (*M*=2.0). Participants reported a perceived effectiveness of the intervention, by indicating an improvement on the domains of their treatment goals (*M*=3.2). On a scale from 0-6, donors reported that the assignments were easily understandable (*M*=5.1), had an appropriate length (*M*=4.4), and were considered useful (*M*=4.4). The user friendliness was evaluated with a 7.0 on a 10-point scale (Table 2).

Table 2. Results pilot study of the ICBT intervention

	Mean ± sd (range)
Generic satisfaction with the ICBT intervention	
I am satisfied with the ICBT intervention (0-10)	7.7 ± 0.8 (6-8)
The intervention met my expectations (1-4)	3.4 ± 0.7 (2-4)
I received appropriate information before the start of the intervention (1-4)	4.v0 ± 0.0 (4-4)
I have faith that the treatment effect would persist on the longer-term (1-4)	3.4 ± 0.9 (2-4)
I would recommend the ICBT intervention to relatives who consider to donate a kidney (1-4)	3.4 ± 1.1 (1-4)
Perceived effectiveness of the intervention	
Due to the intervention, my functioning on the domains of my treatment goals improved	3.2 ± 0.7 (2-4)
Dedication to the intervention	
During the intervention, I conducted all the assignments completely (1-4)	3.0 ± 1.1 (1-4)
I worked vey intensively on my treatment goals (1-4)	3.3 ± 0.7 (2-4)
I practiced and integrated the learned strategies into daily life (1-4)	3.1 ± 0.4 (2-4)
I made time for the intervention at a fixed moment on the day (1-4)	2.1 ± 0.6 (1-3)
The intervention contributed to an improvement on dealing with problems related to the domains of my treatment goals (1-4)	3.1 ± 0.6 (3-4)
I think the assignments were generally easily understandable (0-6)	5.1 ± 1.4 (2-6)
I think the assignments had an appropriate length (0-6)	4.3 ±1.0 (3-6)
I think the assignments were useful (0-6)	4.4 ± 1.1 (3-6)
Which grade would you give to the user friendliness of the website? (1-10)	7.0 ± 1.4 (4-8)
The therapeutic relationship	
Working alliance (WAI)	
Agreement on therapy goals (1-5)	4.2 ± 0.6 (3.0-.4.8)
Agreement on therapy tasks (1-5)	3.8 ± 1.0 (1.8-4.8)
Relational bond between patient and therapist(1-5)	4.4 ± 0.6 (3.5-5.0)
Internet-specific aspects of the therapeutic relationship **(ITRQ)**	
The time lag aspects of communication and receiving sufficient attention from the E-coach therapist (1-10)	8.9 ± 1.1 (7.5-10.0)
Sharing of information with the therapist and the home as the treatment environment (1-10)	7.8 ± 2.2 (5.0-10.0)

ITRQ, Internet-Specific Therapeutic Relationship Questionnaire. WAI, Working Alliance Inventory.

The therapeutic relationship during the ICBT intervention was evaluated very positively, with a high agreement on therapy goals (*M*=4.2) and on therapy tasks (*M*=3.8), and the development of a strong relational bond between patient and therapist (*M*=4.4) on a 1-5 scale. Also, internet-specific aspects of the therapeutic relationship were rated very positively, such as the ITRQ subscale 'Internet-specific time and attention' that describes time lag aspects of communication and receiving sufficient attention from the ICBT therapist (*M*=8.9), and the subscale 'Internet-specific reflection and comfort' that includes the sharing of information with the therapist and the home as the treatment environment (*M*=7.8) on a 1-10 scale (Table 2).

Usage of the ICBT intervention

Concerning the usage of the ICBT intervention by donors, the mean number of logins per donor was *M*=29.1 (range=3-55), with a duration of *M*=9.4 minutes per login (range 0.5-128). The number of assignments that was completed by donors was *M*=22.9 (range 5-36), and the mean number of messages they sent to their therapist was *M*=13.6 (range 1-24). The mean total intervention duration was *M*=7.1 hours (range 0.7-19.7 hours).

With regard to the usage of the website by the psychologist who guided the intervention, the mean time duration of one login of the therapist was *M*=47.0 minutes. The therapist sent an average of 15 (range 3-25) messages per donor.

DISCUSSION

In the present study, a therapist-guided internet-based CBT intervention was developed, tailored to the specific needs of (potential) kidney donors. The feasibility and perceived effectiveness of the intervention was evaluated in a small group of (potential) kidney donors, showing positive evaluations with regard to satisfaction with the intervention, perceived effectiveness, user-friendliness, and therapeutic relationship.

An existing tailored ICBT intervention that has been found effective in patients with different somatic conditions (27, 29) was slightly adapted to the specific characteristics of the donor population, based on focus group interviews. Relevant themes deduced for the content of the intervention included physical difficulties, work resumption problems, and emotional and social-relational problems. Accordingly, donor-specific treatment modules, assignments, and psycho-educational texts on the themes that were derived from the focus group interviews were included in the ICBT intervention. The attitude towards an internet-based intervention for (potential) kidney donors was mainly positive. After a first short screening on elevated levels of psychological distress, a small, but representative group of (potential) kidney donors with a higher risk profile followed and evaluated the ICBT intervention. Participants were satisfied about the information provi-

sion, the content, and the usefulness of the ICBT intervention, and were very positive about the possibility to build a strong relationship with their therapist. Also, the user friendliness was evaluated positively and participants indicated an improvement on the domains of their treatment goals. Thus, this pilot study provides promising indications for a useful and acceptable potential addition to psychosocial care for kidney donors.

The use of web-based interventions in healthcare has been increasing during the last decades. For (potential) kidney donors, web-based interventions could be very suitable by saving time and costs related to travelling towards the transplantation center. The positive evaluation of the ICBT intervention could be a result of the tailored intervention approach, which has the advantage of matching the intervention to the needs and characteristics of that specific donor. Both the focus groups interviews in the current study as well as previous literature indicated that most kidney donors experience no or a limited degree of problems before or after donation. However, when (potential) kidney donors do experience difficulties, these are mostly very specific for the situation of that donor and it is hard to develop a generic intervention protocol that could be used for all donors. With the tailoring approach, each kidney donor at risk can receive the optimal intervention. Also, the very positive evaluation of the contact with the therapist could have contributed to the positive evaluation of the guided ICBT intervention by (potential) kidney donors.

Due to the novelty of the internet-based approach of donor coaching, the current study was conducted in a small group of (potential) kidney donors, to test the satisfaction and feasibility of the newly developed intervention. In future research, the ICBT intervention should be evaluated in a larger sample of (potential) kidney donors. Furthermore, the current study merely focused on the subjective evaluation of the intervention to examine its feasibility before applying it to a larger donor population. In the next step, it would be useful to demonstrate the effectiveness of the intervention in comparison to usual psychosocial care for (potential) kidney donors, assessing pre- and post-intervention outcomes prospectively (27, 29).

(Potential) Kidney donors with mild to moderate levels of distress were invited to follow the ICBT intervention. Some donors indicated that they experienced only minor difficulties, and were therefore not interested in following the intervention. In future research, valid cut-off criteria to screen for psychological distress have to be examined, to formulate evidence-based inclusion criteria. Also, for the participation in ICBT interventions, general computer skills as well as some knowledge on the use of internet are necessary.

In conclusion, from the donor perspective the newly developed ICBT intervention was developed based on the results of focus groups and evaluated positively, both in terms of feasibility (procedure, content, user-friendliness) and perceived effectiveness.

Future research should examine the added value of the intervention and the possibility to integrate it into the current psychosocial care for kidney donors.

REFERENCES

1. Jowsey SG, Jacobs C, Gross CR, Hong BA, Messersmith EE, Gillespie BW, et al. Emotional well-being of living kidney donors: findings from the RELIVE Study. Am J Transplant. 2014; 14: 2535-2544.
2. Timmerman L, Timman R, Laging M, Zuidema WC, Beck DK, JN IJ, et al. Predicting mental health after living kidney donation: The importance of psychological factors. Br J Health Psychol. 2016; 21: 533-554.
3. Smith GC, Trauer T, Kerr PG, Chadban SJ. Prospective psychosocial monitoring of living kidney donors using the Short Form-36 health survey: results at 12 months. Transplantation. 2004; 78: 1384-1389.
4. Wirken L, van Middendorp H, Hooghof CW, Sanders JSF, Dam RE, van der Pant KAMI, et al. Consequences of living kidney donation: a prospective multicenter study. submitted.
5. Wirken L, van Middendorp H, Hooghof CW, Rovers MM, Hoitsma AJ, Hilbrands LB, et al. The Course and Predictors of Health-Related Quality of Life in Living Kidney Donors: A Systematic Review and Meta-Analysis. Am J Transplant. 2015; 15: 3041-3054.
6. Gross CR, Messersmith EE, Hong BA, Jowsey SG, Jacobs C, Gillespie BW, et al. Health-related quality of life in kidney donors from the last five decades: results from the RELIVE study. Am J Transplant. 2013; 13: 2924-2934.
7. Clemens B, Menes A, Piros P, Bessenyei M, Altmann A, Jerney J, et al. Quantitative EEG effects of carbamazepine, oxcarbazepine, valproate, lamotrigine, and possible clinical relevance of the findings. Epilepsy Res. 2006; 70: 190-199.
8. Tong A, Chapman JR, Wong G, Kanellis J, McCarthy G, Craig JC. The motivations and experiences of living kidney donors: a thematic synthesis. Am J Kidney Dis. 2012; 60: 15-26.
9. Tong A, Chapman JR, Wong G, de Bruijn J, Craig JC. Screening and follow-up of living kidney donors: a systematic review of clinical practice guidelines. Transplantation. 2011; 92: 962-972.
10. Duerinckx N, Timmerman L, Van Gogh J, van Busschbach J, Ismail SY, Massey EK, et al. Predonation psychosocial evaluation of living kidney and liver donor candidates: a systematic literature review. Transpl Int. 2014;27: 2-18.
11. Lidobs recommendations Barcelona. 2014.
12. Bahler CD, Sundaram CP. Quality of life following laparoscopic living-donor nephrectomy. JSLS. 2013; 17: 273-278.
13. Rodrigue JR, Pavlakis M, Egbuna O, Paek M, Waterman AD, Mandelbrot DA. The "House Calls" trial: a randomized controlled trial to reduce racial disparities in live donor kidney transplantation: rationale and design. Contemp Clin Trials. 2012; 33: 811-818.
14. Dew MA, DiMartini AF, DeVito Dabbs AJ, Zuckoff A, Tan HP, McNulty ML, et al. Preventive intervention for living donor psychosocial outcomes: feasibility and efficacy in a randomized controlled trial. Am J Transplant. 2013; 13: 2672-2684.
15. Jacobs CL, Gross CR, Messersmith EE, Hong BA, Gillespie BW, Hill-Callahan P, et al. Emotional and Financial Experiences of Kidney Donors over the Past 50 Years: The RELIVE Study. Clin J Am Soc Nephrol. 2015; 10: 2221-2231.
16. Matas AJ, Hays RE, Ibrahim HN. Long-Term Non-End-Stage Renal Disease Risks After Living Kidney Donation. Am J Transplant. 2017; 17: 893-900.
17. Butler AC, Chapman JE, Forman EM, Beck AT. The empirical status of cognitive-behavioral therapy: a review of meta-analyses. Clin Psychol Rev. 2006; 26: 17-31.
18. Hofmann SG, Asnaani A, Vonk IJ, Sawyer AT, Fang A. The Efficacy of Cognitive Behavioral Therapy: A Review of Meta-analyses. Cognit Ther Res. 2012; 36: 427-440.

19. Andersson G, Cuijpers P, Carlbring P, Riper H, Hedman E. Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. World Psychiatry. 2014; 13: 288-95.
20. Cuijpers P, van Straten A, Andersson G. Internet-administered cognitive behavior therapy for health problems: a systematic review. J Behav Med. 2008; 31: 169-177.
21. van Beugen S, Ferwerda M, Hoeve D, Rovers MM, Spillekom-van Koulil S, van Middendorp H, et al. Internet-based cognitive behavioral therapy for patients with chronic somatic conditions: a meta-analytic review. J Med Internet Res. 2014; 16:e88.
22. Johansson R, Andersson G. Internet-based psychological treatments for depression. Expert Rev Neurother. 2012; 12: 861-869; quiz 70.
23. Andersson G. The promise and pitfalls of the internet for cognitive behavioral therapy. BMC Med. 2010; 8: 82.
24. Newman MG, Szkodny LE, Llera SJ, Przeworski A. A review of technology-assisted self-help and minimal contact therapies for anxiety and depression: is human contact necessary for therapeutic efficacy? Clin Psychol Rev. 2011; 31: 89-103.
25. Johansson R, Sjoberg E, Sjogren M, Johnsson E, Carlbring P, Andersson T, et al. Tailored vs. standardized internet-based cognitive behavior therapy for depression and comorbid symptoms: a randomized controlled trial. PLoS One. 2012; 7: e36905.
26. Turk DC. Customizing treatment for chronic pain patients: who, what, and why. Clin J Pain. 1990; 6: 255-270.
27. van Beugen S, Ferwerda M, Spillekom-van Koulil S, Smit JV, Zeeuwen-Franssen ME, Kroft EB, et al. Tailored Therapist-Guided Internet-Based Cognitive Behavioral Treatment for Psoriasis: A Randomized Controlled Trial. Psychother Psychosom. 2016; 85: 297-307.
28. Ferwerda M, van Beugen S, van Burik A, van Middendorp H, de Jong EM, van de Kerkhof PC, et al. What patients think about E-health: patients' perspective on internet-based cognitive behavioral treatment for patients with rheumatoid arthritis and psoriasis. Clin Rheumatol. 2013; 32: 869-873.
29. Ferwerda M, van Beugen S, van Middendorp H, Spillekom-van Koulil S, Donders ART, Visser H, et al. A tailored-guided internet-based cognitive-behavioral intervention for patients with rheumatoid arthritis as an adjunct to standard rheumatological care: results of a randomized controlled trial. Pain. 2017; 158: 868-878.
30. Hays RD, Morales LS. The RAND-36 measure of health-related quality of life. Ann Med. 2001; 33: 350-357.
31. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983; 67: 361-370.
32. Vercoulen JH, Swanink CM, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G. Dimensional assessment of chronic fatigue syndrome. J Psychosom Res. 1994; 38: 383-392.
33. Costa PT, Jr., McCrae RR. Domains and facets: hierarchical personality assessment using the revised NEO personality inventory. J Pers Assess. 1995; 64: 21-50.
34. Boyce P, Parker G. Development of a scale to measure interpersonal sensitivity. Aust N Z J Psychiatry. 1989; 23: 341-351.
35. Dam-Baggen R. De Inventarisatielijst Sociale Betrokkenheid (ISB): een zelfbeoordelingslijst om sociale steun te meten (Inventory for social reliance (ISR): a self-report inventory for the measurement of social support). Gedragstherapie. 1992; 25: 27-46.
36. Busseri MA, Tyler JD. Interchangeability of the Working Alliance Inventory and Working Alliance Inventory, Short Form. Psychol Assess. 2003; 15: 193-197.

37. Horvath. Development and validation of the Working Alliance Inventory. J Couns Psychl. 1989; 36: 223-233.
38. Ferwerda M, van Beugen S, van Riel PC, van de Kerkhof PC, de Jong EM, Smit JV, et al. Measuring the Therapeutic Relationship in Internet-Based Interventions. Psychother Psychosom. 2016; 85: 47-49.

Chapter 7

English Summary

Living donor kidney transplantation is currently the preferred treatment for patients with end-stage renal disease, because of a better health-related quality of life (HRQoL) after transplantation than during dialysis treatment, and higher patient and graft survival rates as compared to deceased donor kidney transplantation. Most living kidney donors experience only temporary physical limitations after surgery and do not encounter sustained difficulties in physical or psychosocial functioning at the longer-term. However, previous research shows that a subgroup of donors experiences donation-related adjustment problems during or after the donation procedure, such as anxiety or fatigue. To date, no evidence-based guidelines exist to identify donors at risk of developing adjustment problems after donation, due to the limited number of large prospective prediction studies available. Therefore, the psychosocial donor evaluation is now mainly based on the clinical judgments of transplant professionals. The prognostic value of these judgments is currently unknown. Furthermore, no interventions for donors with a risk profile or donors who experience adjustment problems are available.

Consequently, the main purpose of the research performed in this thesis was to assess and identify potential risk and resilience factors for longer-term impaired donor functioning, resulting in a psychosocial screening instrument. This screening can be used to identify donors at risk who might need additional psychosocial support during the donation procedure. Secondly, a tailored internet-based intervention for donors at risk of longer-term adjustment problems was developed and evaluated in a small group of donors.

Chapter 2 of this thesis comprises a systematic review and meta-analysis summarizing the existing literature on HRQoL of living kidney donors. Both the current state-of-knowledge on the course of HRQoL from before to after donation and potential risk factors for poorer longer-term functioning after donation were described. Results indicated that HRQoL of donors (i.e., physical, psychological, and social-relational functioning) was comparable with or sometimes even better than that of the general population before donation. HRQoL decreased shortly after donation (1-2 months after donation). During the first year after donation, HRQoL generally returned to baseline levels or remained slightly reduced, which was particularly reflected in elevated levels of fatigue. Concerning risk factors for poorer longer-term functioning after donation, a limited number of prospective prediction studies was available, describing a large variety of potential predictors in relatively small study cohorts. From these studies, baseline psychological functioning was considered to be the most consistent predictor for longer-term HRQoL after donation. However, the review also demonstrated that more systematic research on a comprehensive set of potential predictors of longer-term HRQoL after donation in large research samples is required to develop reliable screening tools.

In **Chapter 3**, the results of a prospective study in a large group of kidney donors from seven Dutch transplantation centers are presented on the course of HRQoL on three dif-

ferent time points; before donation, 6 and 12 months after donation. Both generic quality of life instruments as well as donation-specific questionnaires were applied to examine a systematic overview of donor's HRQoL. The generic HRQoL assessments indicated that donor physical HRQoL was comparable before and after donation, but fatigue levels were somewhat elevated up to twelve months after donation. Mental HRQoL decreased up to six months after donation, but returned to baseline levels at twelve months after donation. Clinically relevant HRQoL changes between the three assessment points were only found for fatigue. These results were in line with those of previous studies, as was described in our meta-analysis (Chapter 2). Concerning donation-specific measurements, the experienced longer-term physical and relational consequences of donation were limited, although many donors reported some degree of post-donation worries, and 14% of donors reported feelings of regret towards the donation decision. Related donors perceived a strong improvement of physical and emotional functioning of their recipient by the donation, and their own life was less influenced by the recipient's kidney disease after transplantation. The donor-recipient relationship was perceived positively at all time points. To conclude, both generic and donation-specific measures offer valuable information about the course of HRQoL before and after living kidney donation and generally provide a positive view on the impact of the kidney donation on the wellbeing of the donor. However, somewhat elevated fatigue levels were experienced after donation, and a small number of donors reported post-donation worries and feelings of regret about the donation decision.

Guidelines on psychosocial evaluation mostly include the assessment of the decision-making process about the donation, by examining the donor's motivation for donation, the expectations of donation and potential worries about the donation. However, there were no validated tools to assess all these potential cognitions regarding organ donation using one questionnaire. Therefore, in **Chapter 4**, a new questionnaire to measure pre-donation cognitions about the donation (i.e., the motivation for donation, the expectations of donation, and worries about donation) was developed and validated in a large group of potential kidney donors from seven Dutch transplantation centers (The Donation Cognition Instrument (DCI). The 31-item questionnaire was found to consist of five categories of cognitions, namely donor benefits, recipient benefits, idealistic incentives, expectations of gratitude, and worries about donation. Cognitions about recipient benefits were most commonly reported and cognitions about the donor's own benefit least commonly. The questionnaire was found to be a reliable psychometric instrument, as indicated by high internal consistency among the subscale items. Furthermore, small to moderate relationships between pre-donation cognitions and HRQoL were found, which supports the validity and endorses the potential added value of this new instrument for psychosocial evaluation in potential living organ donors.

To date, no systematic evaluation of potentially relevant predictors has been conducted, including both donor demographic, medical, and psychosocial factors (e.g., pre-donation cognitions) pre-, intra- and post-donation, and recipient characteristics. Consequently, the psychosocial donor evaluation is currently mainly based on the clinical judgments of transplant professionals, of which the accuracy is unknown. **Chapter 5** describes the effectiveness of the psychosocial donor evaluation by transplant professionals, and the potential value of donor self-report measures in optimizing this psychosocial evaluation. Next to clinical risk assessments by transplant professionals, the role of a comprehensive account of pre-, intra-, and post-donation characteristics of the donor, and donor self-report measures in the prediction of impaired longer-term HRQoL of living kidney donors was examined. Results indicated that clinical judgments of transplant professionals predicted a significant part of the longer-term HRQoL of donors, which endorses the current psychosocial donor evaluation. Furthermore, the addition of donor self-report questionnaires significantly increased the explained variance in HRQoL after donation as compared to the clinical judgments of transplant professionals alone, with baseline physical and psychological functioning being the most important predictors. Combining clinical judgments and self-report questionnaires explain short- and longer-term post-donation HRQoL. Consequently, the integration of donor self-report measures in the current psychosocial donor evaluation by transplant professionals could optimize the psychosocial donor evaluation. Knowledge on the most important risk factors for impaired longer-term donor HRQoL could identify donors with a high-risk profile, who could benefit from additional support during the donation procedure in order to prevent or minimize post-donation adjustment problems.

As a follow-up of the identification of risk factors for longer-term adjustment problems, evidence-based interventions are needed to provide additional psychosocial support for donors at risk. **Chapter 6** describes the transition from donor assessment to donor intervention, and comprises the development and evaluation of a guided and tailored internet-based cognitive behavioral (ICBT) intervention for (potential) donors with a high-risk profile. Based on literature review and focus group interviews with donors and transplant professionals, an existing ICBT intervention for patients with somatic conditions was adjusted to make it feasible for the donor population, including specific donation-relevant topics such as decision-making regarding the donation, returning to daily life, feelings of guilt, and social-relational difficulties after donation. This ICBT intervention was developed for donors with a high-risk profile, indicated by elevated levels of adjustment problems using a short screening questionnaire. In a small pilot study, eight (potential) donors received a face-to-face consultation with their therapist, in which treatment goals were formulated, after which the intervention was offered via the internet. Donors evaluated the feasibility and perceived effectiveness of this intervention positively. These promising results demonstrate that an evidence-

based psychosocial screening and intervention protocol could be easily implemented in clinical practice, because no standardized psychosocial care is currently structurally available for this group.

In conclusion, the studies described in this thesis demonstrate that HRQoL of living kidney donors is generally reduced shortly after donation, but is mostly comparable to general population norms at the longer-term after donation. Clinically relevant HRQoL changes between the three assessment points were only found for fatigue. The current psychosocial donor evaluation by transplant professionals is able to predict longer-term physical and psychological wellbeing of donors. The incorporation of donor self-report measures could optimize this psychosocial evaluation by transplant professionals. Poorer baseline physical and psychosocial functioning are the most consistent predictors for longer-term adjustment problems, but also cognitions around the donation decision, medical factors, and social-relational characteristics could be useful to be included in the donor eligibility screening, in order to offer concrete suggestion on how to intervene. Based on this study, it could be recommended to include a short screening on pre-donation physical and psychosocial functioning to the psychosocial donor evaluation. When a donor would show an elevated risk of developing longer-term adjustment problems based on this screening, a more extensive questionnaire assessment could be feasible, to identify specific areas of functioning that could benefit from additional support during the donation procedure. For donors with a high-risk profile, tailored ICBT interventions seem a promising addition to current donor care, to provide additional psychosocial guidance during the donation procedure. Future research should examine the (cost)-effectiveness of the developed intervention and the possibilities of implementation of the psychosocial screening in current psychosocial donor care.

Chapter 8

General discussion

There is an ongoing disparity between the number of transplantable donor kidneys that are needed, and the supply of organs from deceased donors. Because of this donor shortage, and due to better transplantation outcomes for the recipient, the number of living donor kidney transplantations has increased in recent years (1). While most living kidney donors recover well after surgery, a subgroup experiences adjustment problems during or after the donation procedure (2, 3).

Due to the scarcity of large prospective studies examining predictors of longer-term impaired donor functioning, the psychosocial donor evaluation is nowadays mainly based on the clinical judgment of transplant professionals. However, the prognostic value of these judgments is currently unknown. Furthermore, there are almost no evidence-based interventions available for donors who experience donation-related problems during the donor eligibility screening procedure or after donation. Consequently, the studies described in this thesis focus on the comprehensive assessment and identification of risk and resilience factors for longer-term impaired donor functioning (Chapters 2-5), and on the development of an intervention for donors with a high-risk profile (Chapter 6). The main findings of the studies described in this thesis are summarized in Chapter 7. The current chapter discusses the methodological considerations, recommendations for future research, and clinical implications of the findings.

The course of health-related quality of life before and after donation

In Chapter 2 of this thesis, a systematic evaluation of results of previous studies on HRQoL before and after kidney donation is provided. Results indicate that HRQoL (e.g., physical, psychological, and social-relational functioning) is lower during the early postoperative recovery period. During the first year after donation, HRQoL generally returns to baseline levels or remains slightly reduced, the latter of which was particularly reflected in elevated fatigue levels. Despite this slight decrease in different aspects of functioning, longer-term HRQoL is still comparable to population norms, due to the relatively high HRQoL levels before donation in this population.

Previous studies mostly used generic HRQoL instruments, and did not capture specific relevant donation-related domains of donor functioning prospectively (2, 12, 13). Therefore, in Chapter 3 of this thesis, both generic and donation-specific prospective measurements are used to describe the HRQoL course from before donation up to twelve months after donation in a large group of kidney donors. In line with previous studies, as were summarized in our meta-analysis in Chapter 2, generic HRQoL showed a temporary decrease shortly after donation, but returned to baseline levels within 12 months after donation, with the exception of fatigue. Combined with the relatively limited physical and relational consequences of donation and the positive consequences regarding recipient functioning and the diminished impact of the disease on the donor's life, this indicates that in general donation has no major long-term negative

HRQoL consequences. These donor outcomes, together with the expected beneficial clinical outcomes for the recipient supports the use of living donors for transplantation. The cause of the elevated fatigue levels remained unclear, and needs to be studied in future research. Potential factors influencing fatigue are ageing, living with one kidney, or too early resumption of daily activities by donors who are not familiar with physical limitations. This finding of heightened fatigue levels in donors indicates the need to specifically monitor fatigue after donation and to target fatigue in interventions, for example by cognitive behavioral therapy. Despite the fact that HRQoL is not negatively affected in most donors, some donors do experience longer-lasting HRQoL deteriorations, worries, or regret after donation. For this subgroup, it is relevant to know the most relevant predictors of such adjustments problems, in order to enable prevention or early identification and treatment of donors at risk.

The percentage of donors that reported substantial feelings of regret about the donation decision was somewhat higher in the current study than in previous research (≤14% versus 6%) (14-18). Previously, regret about the donation was mostly examined by qualitative research methods using interviews, or using a single question about the presence of feelings of regret about the donation during donor follow-up (19). In the current study, the Decision Regret Scale was applied, which is a multidimensional quantitative assessment method. This instrument was previously used in different populations measuring regret after healthcare decisions (e.g., menopausal women deciding whether or not to choose hormone replacement therapy, and breast cancer patients deciding whether or not to proceed with adjuvant therapy after the primary surgical intervention). Regret scores of these patient populations were in the same range as the percentage of donors that experienced substantial feelings of regret. The results suggest that using this multidimensional measurement of regret potentially provides more information about the extent to which donors experience regret.

The results on the course of HRQoL indicate that psychosocial follow-up consultations might be advisable for donors experiencing adjustment problems. Currently, the extent to which psychosocial follow-up care is available for living kidney donors differs between transplantation centers. Some centers provide standard psychosocial follow-up, while others offer the possibility to contact the transplantation center in the event that a donor experiences difficulties. The results of studies showing that donor subgroups experience psychosocial problems after donation, justify the importance of psychosocial follow-up appointments with medical social workers or psychologists for donors who experience donation-related problems. In order to prevent or treat these problems at an early stage, it is relevant to identify donors at risk of longer-term psychosocial problems by means of a psychosocial donor evaluation either before or after donation.

Donor risk assessment

In this thesis, an encompassing psychosocial screening instrument is developed and validated. As part of this screening instrument, different pre-donation cognitions could be identified using the newly developed Donation Cognition Instrument (DCI), namely cognitions about donor and recipient benefits, idealistic incentives, expectations of gratitude, and worries about donation. The systematic assessment of these cognitions could be a valuable addition to generic pre-donation HRQoL measures in facilitating psychosocial donor evaluation by healthcare professionals, and could provide themes for discussion during donor counseling.

In line with the limited number of prospective prediction studies in kidney donation samples as summarized in our meta-analysis (Chapter 2), worse baseline physical and psychological functioning were found to be the strongest predictors of impaired HRQoL in the longer term after donation when taking an comprehensive set of pre-, intra-, and post-donation socio-demographic, medical, and self-report predictors into account. It might be advisable to include these potential risk factors in donor screening, using a short screening on baseline physical and psychosocial functioning, and a more extended assessment to identify specific problem areas in high-risk donors.

Psychosocial donor assessments early in the donation procedure may improve awareness of elevated donation-related distress levels, and provide an early identification of potential donors at risk of longer-term adjustment problems after donation. In this way, donors with a high-risk profile could be offered additional psychosocial care during or after the donation procedure to prevent the onset or deterioration of longer-term donation-related distress.

Psychosocial screening could provide pro-active care to patients instead of reactive care as a part of personalized medicine to identify vulnerable patients in an early stage. Also, it could facilitate the communication about mental health problems between patients and healthcare providers, and could therefore be efficient and effective in preventing longer-term problems (20). The results from the studies reported in this thesis are promising in enabling improved psychosocial risk assessment of potential donors. Besides the advantages of psychosocial donor assessments, there are also some possible hindering factors, such as the personnel costs involved in interpreting screening results and guiding donors at risk, the time investment of donors and potential donors, and potential false-positive results that require follow-up. Future research into the specificity and sensitivity of adding a short stepwise screening tool to the psychosocial donor evaluation in practice, in order to allow early identification of donors with a high-risk profile, should show whether the advantages weigh up to the disadvantages and provide a cost-effective means to prevent psychosocial problems on the longer-term after kidney donation (21).

Donor risk assessment by transplant professionals

Because of the low number of large prospective prediction studies on the identification of risk factors for impaired longer-term functioning, the psychosocial donor evaluation is currently mainly based on the clinical judgments of transplant professionals. These judgments are generally based on one or two consultations with the donor. Impaired longer-term physical functioning of donors was predicted by higher risk estimations of all transplant professionals, while impaired longer-term psychological functioning could be predicted by medical social workers, but not by nephrologists and donation coordinating nurses. This suggests that the global estimation of physical functioning or limitations could be conducted by all disciplines, but that donors could be reluctant to disclose mental health concerns to their physician and may prefer to share these problems with medical social workers. However, these differences could also be caused by the fact that physicians and coordinating nurses have limited time to discuss psychosocial issues during their consultations (22), or the idea of donor candidates that they will be rejected to donate when they disclose mental health concerns with physicians. Future research should disentangle the specific components of the clinical consultations of different health professionals that are necessary to assess a valid physical or psychosocial risk profile.

The finding that donor self-report questionnaires added significantly to the explained variance in HRQoL after donation is in accordance with results of previous research, stating that so-called patient-reported outcomes or PROs are an important addition to medical care, because they offer patients the opportunity to express their own subjective perception of their health and wellbeing (23, 24). Also, when these patient-reported outcomes are assessed repeatedly, they could be useful to evaluate the subjective benefit of medical procedures for patients (25-27).

Psychosocial interventions

Previous studies and our current prospective study have concluded a possible added value of psychosocial interventions for living kidney donors who experience psychosocial adjustment problems during or after the donation procedure (28-30). Currently, however, the number of interventions that are available for donors is very limited. This is potentially caused by the donation-specific problems that are reported by donors, which makes it difficult to build on existing interventions. Also, donation-related problems differ between donors, asking for a personalized approach in donor interventions, tailoring the intervention to the needs of the specific donor. Previous research indicated several advantages of internet-based interventions in comparison to face-to-face consultations, such as reduced travelling time and costs, following the intervention from one's own home, and reducing potential barriers to seeking psychological support from mental health providers as well as possible higher cost-effectiveness (31). As concluded from

previous research, tailoring interventions to patient and disease characteristics, therapeutic guidance and optimal timing of the intervention could enhance the effectiveness of the treatment (32, 33).

The positive evaluation of the feasibility and perceived effectiveness of a guided and tailored ICBT intervention incorporating specific donation-related topics in a small group of donors (Chapter 6) show the potential added value of tailored and guided interventions for donors with a high-risk profile. As this study did not compare the tailored and guided approach to a non-tailored and non-guided approach, it is still unknown whether the perceived effectiveness of the intervention is attributable to these working mechanisms and has to be examined in future studies.

Methodological considerations

Although overall promising, the results of the studies described in this thesis warrant careful consideration. First, the current prospective study on the course of HRQoL did not include a control group with which to compare the results of psychosocial functioning before and after donation. A reliable control group for the donor population is difficult to select. For example, donors are not comparable to the general population, because they are generally healthier than the normal population when they are perceived as suitable donors and surgery is planned (34, 35). After surgery, their health is temporarily worse than before donation because of the recovery from surgery. Donors who were eligible for donation but did not donate may not be representative because potential psychosocial or physical factors could have influenced the decision to stop the donation procedure. Finally, potential donors who are excluded from donation are not a reliable control group because exclusion from donation is found to have a major impact on the psychosocial functioning of rejected donors, for example leading to the experiencing of feelings of guilt towards their intended recipient (36).

Second, the current study aimed to examine the predictive value and relative contribution of a comprehensive number of predictors on longer-term HRQoL in living kidney donors. Although the sample size of the current study was relatively large, more statistical power might be needed to examine the predictive value of all possible relevant predictors. Also, differences between subgroups of donors regarding potential predictors of longer-term HRQoL (e.g., different donor-recipient relationships) could not be reliably examined because of the small sample sizes of these different subgroups. Future research should examine potentially different predictors of longer-term HRQoL in these subgroups, to determine whether screening instruments have to be tailored to different donor subgroups. Furthermore, due to the limited number of surgical complications in donors and recipients, the predictive value of these complications on longer-term HRQoL could not be examined reliably in the current study. As previous studies have indicated them as potential risk factors for impaired longer-term HRQoL, a donor who

experiences complications after surgery or whose recipient experiences complications might be monitored as a potential high-risk donor, so that additional psychosocial care can be provided if this is needed.

Third, despite the large and comprehensive set of pre-, intra-, and postoperative predictors included in the prospective study, there are some potentially relevant predictors of longer-term HRQoL that were not examined in the current study. For example, ambivalence towards the donation decision or the extent to which coercion was experienced by the donor's or recipient's relatives could be potential predictors that have to be studied in future research. Also, including additional objective assessments of donor wellbeing, such as the assessment of donor functioning by donor's relatives, could be valuable in future research.

Fourth, in previous research an interaction between donor and recipient wellbeing before and after the donation was demonstrated (37-40). Although the current study included consequences of donation and transplantation for the recipient as perceived by the donor, no recipient's assessments of their own HRQoL before and after transplantation were included. Future research examining the course of HRQoL of donors and their recipients before and after donation and transplantation could provide more information about the interaction of donor and recipient functioning.

Fifth, the Dutch structure of the donation and transplantation healthcare setting can potentially not be generalized towards those of other countries. In the Netherlands, well-organized regulations are in place on financial compensation for donors. Therefore, the number of donors facing severe financial problems through kidney donation is limited, while negative financial experiences are reported in studies from other countries (41-43).

Sixth, the feasibility of the ICBT intervention and the satisfaction with the intervention were evaluated in a small group of kidney donors. Although the evaluation of the content and structure of the intervention was very promising, future research should examine the effectiveness, including the cost-effectiveness, of the intervention in this population using a randomized controlled trial. Also, longer-term follow-up effects of the intervention should be studied. Lastly, the working mechanisms of the ICBT intervention and the value of tailored versus non-tailored interventions for treatment effects have to be studied, in line with previous studies showing the effectiveness of ICBT interventions in somatic conditions (44). A validated screening tool is also necessary for the application of tailored interventions in order to identify donors at risk and define treatment goals. In the current study, the cut-off values for inclusion in the intervention were relatively mild, so donors with moderate to more severe problems were invited to participate in the intervention to test its feasibility for this group. In future research, the inclusion criteria need to be further validated to include those donors that optimally benefit from the intervention.

Clinical implications

The results of the studies described in the current thesis have several implications for clinical practice.

As impaired baseline physical and psychological functioning were found to be the most consistent predictors of impaired longer-term HRQoL after donation, a first short screening on physical and psychological functioning before donation could be conducted to provide a risk stratification of potential donors (low risk, moderate risk or high risk). If a potential donor experiences poor physical or psychological functioning, additional assessments could be conducted to examine specific problem areas of functioning to focus interventions. Donors could be referred to psychosocial healthcare professionals (e.g., medical social workers or psychologists) to provide additional psychosocial support. Moreover, concerning the elevated fatigue levels found in the longer term after donation in both previous studies and the current study it is important that donors are informed about the potential persistence of fatigue symptoms during the donor eligibility screening. Furthermore, post-donation monitoring of fatigue and providing interventions that focus on (or pay attention to) fatigue could be indicated.

With regard to the timing of psychosocial assessments, it could be useful to include donor assessments at different time points during the donation procedure. Assessments at the start of the donation procedure could examine pre-donation difficulties and identify potential donors at risk early in the donation procedure. Furthermore, at the time surgery is planned, assessments could identify potential cognitions about the surgery that were not experienced earlier in the donation procedure. Lastly, assessments combined with physical monitoring consultations in the hospital after the donation could identify those donors that experience difficulties during the recovery period.

Lastly, in the ICBT treatment, an experienced health psychologist in the area of donation-related difficulties guided the ICBT interventions of the donors, which could have added to the beneficial treatment effects. Because of the specific donation-related problems that occur, therapist experience with the donor population is recommended. Potentially, a stepped-care approach could be feasible for donor psychosocial care (45), in which donors with moderate psychological complaints are guided by medical social workers, and donors with more severe psychosocial symptoms are guided by psychologists.

Future research

Based on the results reported in this thesis, recommendations for future research can be formulated. Potential donors need to receive detailed information about the potential risks and consequences of the donation. Possibly, however, potential donors who have registered in the transplantation centers are not receptive to this information, because they have already made the decision to donate and are reluctant to reconsider this deci-

sion in the context of the potential risks of donation (45, 46). The actual decision-making process probably occurs earlier, and it is difficult to evaluate this process because donors are not connected to the transplantation centers at that point in time (47). As ambivalence towards the donation decision has been found in previous studies to be a potential predictor of impaired longer-term donor functioning (48), it is relevant to study this decision-making process more extensively, for example by means of interviews or questionnaire studies on donors who consider to donate. Possible donors could be recruited by websites providing information about kidney donation procedures and consequences.

As in most studies in living kidney donors, we used self-report assessments of predonation cognitions and HRQoL before and after donation. Structured donor assessments could reveal the presence of contra-indications for donation, such as severe psychiatric comorbidity. There is currently no global consensus on absolute and relative contra-indications for donation, and more long-term prospective prediction studies could provide useful information regarding this issue. Moreover, the concealment of information about potential contra-indications for donation or the emphasis on desired behaviour during donor eligibility screening consultations could lead to an unrealistically positive donor profile (49). It is known from previous studies that subjective assessments do not always reflect the actual cognitions and behaviour of people, and that their behaviour could also be influenced by implicit (more reflexive, and unconscious) cognitive processes. In future research, implicit cognitions could be assessed as part of the donor eligibility screening. For example, the extent to which donors experience coercion to donate could be assessed (50), to test whether an attentional bias towards coercion-related words could be found in donors who experience coercion. Also, fear about the donor surgery could be assessed (51), to study whether donors with higher levels of fear show more surgery-avoidant behaviour than donors who do not experience fear towards the surgery. It would be interesting to examine whether such more implicit measures would add to the prediction of longer-term HRQoL.

Differences in predictors of longer-term HRQoL between different types of donors were not examined in the current study, partly due to the insufficient size of donor subgroups such as altruistic (anonymous) donors. However, the number of transplantations with kidneys from altruistic donors is increasing. In altruistic donation, anonymity between the donor and the recipient is preserved before surgery (52). By not knowing the recipient, altruistic donors are free of coercion, and do not experience concerns about the recipient's functioning. Generally, altruistic donors are not informed about the health status of the recipient after transplantation in The Netherlands. Most donors and recipients are satisfied with this anonymity (53). However, some altruistic donors or recipients of a kidney from an altruistic donor wish to become acquainted with their recipient or donor after the transplantation. Future research should examine the pros

and cons of sharing information about the wellbeing of altruistic donors and their recipients, and the potential influence of being informed about the health state of the other person on donor and recipient's HRQoL. Second, there is an increase in the number of recipients who do not have a living donor, and post an appeal for potential donors on public social media websites, such as Facebook (54). It would be important to examine in future research whether the HRQoL consequences for these donors and recipients are different from standard donor-recipient couples, and whether specific screening or follow-up procedures for these donors are needed.

The current study assessed consequences of donation for donors and predictors of HRQoL up to twelve months after donation. Future research should examine long-term HRQoL consequences of donation for donors and recipients and predictors for long-term adjustment problems. Furthermore, the generalization of the results found towards living donors of (parts of) other organs (e.g., living liver donors) could be examined.

Concerning interventions for donors with a high-risk profile for long-term adjustment problems, future research should examine the effectiveness, including cost-effectiveness, of internet-based versus face-to-face interventions. Also, whether therapist guidance improves both adherence rates and the effectiveness of the intervention in this population can be assessed by comparing guided versus unguided ICBT, next to the comparisons of internet interventions to more blended care or face-to-face treatments. Furthermore, the application of the intervention for different donor subgroups, e.g. regarding cultural background or educational level, has to be evaluated.

Lastly, besides the donation itself, being excluded from donation due to medical reasons (which involves about half of all donor candidates) could also have negative psychosocial consequences for living donor candidates in the longer term. For example, feelings of guilt towards the recipient and their relatives by being physically unable to donate could influence the wellbeing of registered donors. It would be relevant to examine the consequences of exclusion from donation on longer-term HRQoL of these rejected donors.

CONCLUSIONS

The aim of the research performed in this thesis was to enable identification of potential donors at risk for longer-term adjustment problems early in the donation procedure by developing and validating a psychosocial screening instrument. Furthermore, a tailored and guided internet-based cognitive behavioral therapy intervention to treat donors at risk of longer-term adjustment problems was developed and evaluated. The main conclusions drawn from the studies described in this thesis are as follows:

1) Shortly after donation, health-related quality of life levels of donors are reduced but are generally comparable to general population norms longer after donation. Fatigue levels remain somewhat elevated across donors, but are still in the range of the general population.
2) Higher risk estimations by transplant professionals as well as donor self-report measures of their physical and psychological wellbeing independently contribute to the prediction of impaired longer-term donor health-related quality of life.
3) Incorporating information from donor self-reported measures in the donor screening procedure can improve the identification of donors with a risk profile.
4) Baseline physical and psychosocial functioning are the most consistent predictors for longer-term adjustment problems, but cognitions around the donation decision, medical factors, and social-relational characteristics could also be useful factors for donor screening to identify donors at risk.
5) Tailored internet-based cognitive behavioral therapy interventions for donors with a risk profile seem to be a promising addition to current donor care, as a means of providing additional psychosocial guidance during the donation procedure.

REFERENCES

1. Annual Report Dutch Transplant Foundation. 2016
2. Gross CR, Messersmith EE, Hong BA, et al. Health-related quality of life in kidney donors from the last five decades: results from the RELIVE study. Am J Transplant.2013; 13: 2924-2934.
3. Clemens KK, Thiessen-Philbrook H, Parikh CR, et al. Psychosocial health of living kidney donors: a systematic review. Am J Transplant. 2006; 6: 2965-2977.
4. Rodrigue JR, Schutzer ME, Paek M, Morrissey P. Altruistic kidney donation to a stranger: psychosocial and functional outcomes at two US transplant centers. Transplantation. 2011; 91: 772-778.
5. Jowsey SG, Jacobs C, Gross CR, et al. Emotional well-being of living kidney donors: findings from the RELIVE Study. Am J Transplant. 2014; 14: 2535-2544.
6. Dols LF, Ijzermans JN, Wentink N, et al. Long-term follow-up of a randomized trial comparing laparoscopic and mini-incision open live donor nephrectomy. Am J Transplant. 2010; 10: 2481-2487.
7. Klop KW, Kok NF, Dols LF, et al. Can right-sided hand-assisted retroperitoneoscopic donor nephrectomy be advocated above standard laparoscopic donor nephrectomy: a randomized pilot study. Transpl Int. 2014; 27: 162-169.
8. Kok NF, Alwayn IP, Tran KT, Hop WC, Weimar W, Ijzermans JN. Psychosocial and physical impairment after mini-incision open and laparoscopic donor nephrectomy: A prospective study. Transplantation. 2006; 82: 1291-1297.
9. Nicholson ML, Elwell R, Kaushik M, Bagul A, Hosgood SA. Health-related quality of life after living donor nephrectomy: a randomized controlled trial of laparoscopic versus open nephrectomy. Transplantation. 2011; 91: 457-461.
10. Minnee RC, Bemelman WA, Polle SW, et al. Older living kidney donors: surgical outcome and quality of life. Transplantation. 2008; 86: 251-256.
11. Annual Reports Dutch Transplant Foundation. 2000-2016.
12. Andersen MH, Mathisen L, Veenstra M, et al. Quality of life after randomization to laparoscopic versus open living donor nephrectomy: long-term follow-up. Transplantation. 2007; 84: 64-69.
13. Garcia MF, Andrade LG, Carvalho MF. Living kidney donors--a prospective study of quality of life before and after kidney donation. Clin Transplant. 2013; 27: 9-14.
14. Binet I, Bock AH, Vogelbach P, et al. Outcome in emotionally related living kidney donor transplantation. Nephrol Dial Transplant. 1997; 12: 1940-1948.
15. Fehrman-Ekholm I, Brink B, Ericsson C, Elinder CG, Duner F, Lundgren G. Kidney donors don't regret: follow-up of 370 donors in Stockholm since 1964. Transplantation. 2000; 69: 2067-2071.
16. Frade IC, Fonseca I, Dias L, et al. Impact assessment in living kidney donation: psychosocial aspects in the donor. Transplant Proc. 2008; 40: 677-681.
17. Halverson CM, Wang JY, Poulson M, Karlin J, Crowley-Matoka M, Ross LF. Living Kidney Donors Who Develop Kidney Failure: Excerpts of Their Thoughts. Am J Nephrol. 2016; 43: 389-396.
18. Rodrigue JR, Vishnevsky T, Fleishman A, et al. Patient-Reported Outcomes Following Living Kidney Donation: A Single Center Experience. J Clin Psychol Med Settings; 22: 160-168.2015
19. Brehaut JC, O'Connor AM, Wood TJ, et al. Validation of a decision regret scale. Med Decis Making. 2003; 23: 281-292.
20. Kazak AE, Barakat LP, Askins MA, et al. Provider Perspectives on the Implementation of Psychosocial Risk Screening in Pediatric Cancer. J Pediatr Psychol. 2017; 42: 700-710.

21. Evers AWM, Gieler U, Hasenbring MI, Van Middendorp H. Incorporating biopsychosocial characteristics into personalized healthcare: A clinical approach. Psychother Psychosom. 2014; 83: 148-157.
22. Astin JA, Soeken K, Sierpina VS, Clarridge BR. Barriers to the integration of psychosocial factors in medicine: results of a national survey of physicians. J Am Board Fam Med. 2006; 19: 557-565.
23. Deshpande PR, Rajan S, Sudeepthi BL, Abdul Nazir CP. Patient-reported outcomes: A new era in clinical research. Perspect Clin Res. 2011; 2: 137-144.
24. Snyder CF, Jensen RE, Segal JB, Wu AW. Patient-reported outcomes (PROs): putting the patient perspective in patient-centered outcomes research. Med Care. 2013; 51: S73-79.
25. Black N. Patient reported outcome measures could help transform healthcare. BMJ. 2013; 346: f167.
26. Dawson J, Doll H, Fitzpatrick R, Jenkinson C, Carr AJ. The routine use of patient reported outcome measures in healthcare settings. BMJ. 2010; 340: c186.
27. Marshall S, Haywood K, Fitzpatrick R. Impact of patient-reported outcome measures on routine practice: a structured review. J Eval Clin Pract. 2006; 12: 559-568.
28. Giessing M, Reuter S, Schonberger B, et al. Quality of life of living kidney donors in Germany: a survey with the Validated Short Form-36 and Giessen Subjective Complaints List-24 questionnaires. Transplantation. 2004; 78: 864-872.
29. van Hardeveld E, Tong A. The CARI guidelines. Psychosocial care of living kidney donors. Nephrology (Carlton) 2010; 15 Suppl 1: S80-87.
30. Smith GC, Trauer T, Kerr PG, Chadban SJ. Prospective psychosocial monitoring of living kidney donors using the SF-36 health survey. Transplantation. 2003; 76: 807-809.
31. Ferwerda M, van Beugen S, van Burik A, et al. What patients think about E-health: patients' perspective on internet-based cognitive behavioral treatment for patients with rheumatoid arthritis and psoriasis. Clin Rheumatol. 2013; 32: 869-873.
32. Turk DC. Customizing treatment for chronic pain patients: who, what, and why. Clin J Pain. 1990; 6: 255-270.
33. Johansson R, Sjoberg E, Sjogren M, et al. Tailored vs. standardized internet-based cognitive behavior therapy for depression and comorbid symptoms: a randomized controlled trial. PLoS One. 2012; 7: e36905.
34. Kroencke S, Fischer L, Nashan B, Herich L, Schulz KH. A prospective study on living related kidney donors' quality of life in the first year: choosing appropriate reference data. Clin Transplant. 2012; 26: E418-427.
35. Klop KW, Dols LF, Weimar W, Dooper IM, JN IJ, Kok NF. Quality of life of elderly live kidney donors. Transplantation. 2013; 96: 644-648.
36. Thiessen C, Jaji Z, Joyce M, et al. Opting out: a single-centre pilot study assessing the reasons for and the psychosocial impact of withdrawing from living kidney donor evaluation. J Med Ethics. 2017.
37. Nelson EW, Mone MC, Nelson ET, Hansen HJ, Gawlick U, Alder S. Evolution of trends in the live kidney transplant donor-recipient relationship. Transplant Proc. 2013; 45: 57-64.
38. Jacobs C, Johnson E, Anderson K, Gillingham K, Matas A. Kidney transplants from living donors: how donation affects family dynamics. Adv Ren Replace Ther. 1998; 5: 89-97.
39. de Groot IB, Stiggelbout AM, van der Boog PJ, Baranski AG, Marang-van de Mheen PJ, group PA-s. Reduced quality of life in living kidney donors: association with fatigue, societal participation and pre-donation variables. Transpl Int. 2012; 25: 967-975.

40. Buer LC, Hofmann BM. How does kidney transplantation affect the relationship between donor and recipient? Tidsskr Nor Laegeforen. 2012; 132: 41-43.
41. Chen KH, Yeh LC, Huang HL, et al. Factors Determining Physical and Mental Quality of Life of Living Kidney Donors in Taiwan. Transplant Proc. 2016; 48: 745-748.
42. Jacobs CL, Gross CR, Messersmith EE, et al. Emotional and Financial Experiences of Kidney Donors over the Past 50 Years: The RELIVE Study. Clin J Am Soc Nephrol. 2015; 10: 2221-2231.
43. Mjoen G, Stavem K, Westlie L, et al. Quality of life in kidney donors. Am J Transplant. 2011; 11: 1315-1319.
44. van Beugen S, Ferwerda M, Hoeve D, et al. Internet-based cognitive behavioral therapy for patients with chronic somatic conditions: a meta-analytic review. J Med Internet Res. 2014; 16: e88.
45. Association JWPoTBTSaTR. United Kingdom Guidelines for living donor kidney transplantation.2011
46. Russell S, Jacob RG. Living-related organ donation: the donor's dilemma. Patient Educ Couns. 1993; 21: 89-99.
47. Agerskov H, Bistrup C, Ludvigsen MS, Pedersen BD. Living kidney donation: considerations and decision-making. J Ren Care. 2014; 40: 88-95.
48. Dew MA, DiMartini AF, DeVito Dabbs AJ, et al. Preventive intervention for living donor psychosocial outcomes: feasibility and efficacy in a randomized controlled trial. Am J Transplant. 2013; 13: 2672-2684.
49. Hildebrand L, Melchert TP, Anderson RC. Impression management during evaluation and psychological reactions post-donation of living kidney donors. Clin Transplant. 2014; 28: 855-861.
50. Williams JM, Mathews A, MacLeod C. The emotional Stroop task and psychopathology. Psychol Bull 1996; 120: 3-24.
51. Heuer K, Rinck M, Becker ES. Avoidance of emotional facial expressions in social anxiety: The Approach-Avoidance Task. Behav Res Ther. 2007; 45: 2990-3001.
52. Mamode N, Lennerling A, Citterio F, et al. Anonymity and live-donor transplantation: an ELPAT view. Transplantation. 2013; 95: 536-541.
53. Pronk MC, Slaats D, van der Pant K, et al. Toward a conditional approach to anonymity? An explorative multicenter longitudinal study among anonymous living kidney donors and recipients. Transpl Int. 2017
54. Bramstedt KA, Cameron AM. Beyond the Billboard: The Facebook-Based Application, Donor, and Its Guided Approach to Facilitating Living Organ Donation. Am J Transplant. 2017; 17: 336-340.

Dutch Summary

Publications

PhD Portfolio

Dankwoord (Acknowledgements)

Curriculum Vitae

DUTCH SUMMARY

Chronische nieraandoeningen verlopen in vijf fases, waarbij de nierfunctie steeds verder afneemt en lichamelijke klachten van patiënten ontstaan. De vijfde fase van de nieraandoening wordt ook wel het eindstadium nierfalen genoemd, waarbij de nierfunctie minder dan 10% bedraagt. In deze fase is een nierfunctie-vervangende behandeling noodzakelijk, namelijk dialyse of niertransplantatie. Dialyse is een intensieve behandeling waarbij het bloed gefilterd wordt, waardoor afvalstoffen en overtollig vocht uit het lichaam worden verwijderd. Veel patiënten die dialysebehandeling ondergaan ervaren lichamelijke klachten, moeten een streng dieet volgen en mogen maar een zeer beperkte hoeveelheid vocht innemen; bovendien zorgt deze behandeling niet voor een verbetering van de nierfunctie. Na een niertransplantatie verbetert zowel de nierfunctie als ook de levensverwachting en kwaliteit van leven van de patiënt aanzienlijk meer dan tijdens dialysebehandeling. Daarom is transplantatie momenteel de behandeling van voorkeur voor patiënten met eindstadium nierfalen. Niertransplantatie kan plaatsvinden met een nier afkomstig van een overleden donor of van een levende donor. De uitkomsten van de transplantatie en kwaliteit van leven van de ontvanger zijn over het algemeen beter na levende donor niertransplantatie dan bij transplantatie met een nier van een overleden donor. Ook is de wachtlijst voor een nier van een overleden donor nog steeds erg lang, waardoor patiënten gemiddeld 2 tot 3 jaar op een donororgaan moeten wachten. Levende donor niertransplantaties gaan buiten de wachtlijst om en hierdoor is de wachttijd vaak veel korter en kunnen patiënten voor de start van de dialysebehandeling getransplanteerd worden. Het aantal levende donor niertransplantaties is de laatste decennia sterk toegenomen. In Nederland worden momenteel zelfs meer patiënten getransplanteerd met een nier van levende donor dan met een nier van een overleden donor.

Mensen die zich aanmelden als nierdonor hebben zelf geen direct voordeel van de nierdonatie, maar ondergaan een operatie om een voor hen bekende nierpatiënt (vaak partner, familielid of vriend; relationele donor) of onbekende nierpatiënt (altruïstische donor) te helpen. In het geval van relationele donatie ervaren donoren meestal wel positieve indirecte gevolgen van de nierdonatie, doordat de ontvanger lichamelijk en emotioneel gezien opknapt na de transplantatie en activiteiten die voorheen niet mogelijk waren nu wel weer kunnen plaatsvinden. Uit voorgaand onderzoek is bekend dat de meeste nierdonoren goed herstellen na hun donatie en geen lichamelijke of emotionele klachten ervaren op de langere termijn. Er is echter een kleine groep donoren die wel klachten ervaart voorafgaand aan of na de donatie, zoals spanningsklachten ten aanzien van de operatie of aanhoudende vermoeidheid na de donatie. Om het risico op deze problemen zoveel mogelijk te voorkomen worden mensen die zich aanmelden als donor uitgebreid gescreend om te bepalen of iemand al dan niet voor donatie in

aanmerking komt. Op het gebied van de lichamelijke screening is al veel onderzoek uitgevoerd, maar er is nog zeer beperkt onderzoek verricht naar psychosociale kenmerken waarop donoren zouden moeten worden onderzocht tijdens de screening voor donatie. Ook zijn er geen psychosociale behandelingen beschikbaar voor mensen die problemen ervaren voorafgaand aan of na de donatie.

Het doel van dit proefschrift was om risicofactoren en beschermende factoren voor de ontwikkeling van langere termijn problemen bij nierdonoren te identificeren. Deze factoren zouden kunnen worden geïntegreerd in een screeningsinstrument waarmee bepaald kan worden welke donoren aanvullende ondersteuning nodig hebben gedurende de donatieprocedure. Daarnaast werd een psychosociale behandeling voor donoren met een verhoogd risico op problemen na de donatie ontwikkeld en geëvalueerd in een kleine groep donoren.

In **Hoofdstuk 2** gaven we een overzicht van voorgaande studies naar de kwaliteit van leven van donoren voorafgaand aan en na de nierdonatie. We hebben daarbij zowel de bevindingen ten aanzien van het beloop van kwaliteit van leven (lichamelijk, emotioneel en sociaal functioneren) van donoren van voor tot na de donatie als risicofactoren voor een verminderde kwaliteit van leven na donatie samengevat. De resultaten lieten zien dat de kwaliteit van leven van donoren voorafgaand aan de donatie vergelijkbaar of zelfs beter is dan de algemene populatie. Kort na de donatie (1-2 maanden na de operatie) was de kwaliteit van leven op een lager niveau dan voor de donatie, maar in de maanden daarna keerde deze in het algemeen terug op het niveau van voor de donatie. Een uitzondering hierop was vermoeidheid, waarvan in meerdere studies werd gevonden dat deze na de donatie langer aanhield.

Er waren slechts weinig studies beschikbaar die risicofactoren voor een verminderde kwaliteit van leven na de nierdonatie hadden bestudeerd, en de studies die gedaan waren gingen over kleine groepen donoren en bekeken een grote verscheidenheid aan risicofactoren. Deze studies boden voorzichtige aanwijzingen dat lichamelijk en emotioneel functioneren voorafgaand aan de donatie mogelijk de belangrijkste voorspellers zouden kunnen zijn voor langere termijn kwaliteit van leven na de donatie. Maar om betrouwbare uitspraken te doen over mogelijke factoren die het langere-termijn functioneren van donoren zouden kunnen voorspellen was meer systematisch onderzoek in grotere groepen donoren noodzakelijk. De onderzoeken uitgevoerd in het kader van dit proefschrift zijn daarom hierop gericht.

In **Hoofdstuk 3** onderzochten we het beloop van kwaliteit van leven van voor de donatie tot 1 jaar na de donatie van een grote groep van 230 nierdonoren afkomstig uit zeven Nederlandse transplantatiecentra. Om een zo omvattend mogelijk beeld te krijgen van relevante aspecten van kwaliteit van leven die spelen rondom nierdonatie bij leven werden hierbij zowel algemene vragenlijsten naar kwaliteit van leven gebruikt

als ook meer donatie-specifieke vragenlijsten. Uit de algemene kwaliteit van leven vragenlijsten kwamen vergelijkbare resultaten als uit het overzicht van eerder onderzoek was gebleken. Zo bleek dat het algemene lichamelijke functioneren van donoren vergelijkbaar was tussen de drie meetmomenten, maar dat donoren 6 en 12 maanden na de donatie meer vermoeid waren dan voor de operatie. Ook bleek het emotioneel functioneren van de donoren 6 maanden na donatie verminderd te zijn ten opzichte van voor de donatie, maar was deze na 1 jaar teruggekeerd op het niveau van voor de donatie. Klinisch relevante veranderingen in kwaliteit van leven werden alleen gevonden voor vermoeidheid. Uit de donatie-specifieke vragenlijsten bleek dat de lichamelijke veranderingen en veranderingen in de relatie tussen de donor en ontvanger na de donatie beperkt waren, maar dat de meerderheid van de donoren zich op bepaalde momenten na de donatie zorgen hebben gemaakt over zichzelf of de ontvanger. Een aantal donoren rapporteerde 1 jaar na donatie gevoelens van spijt rondom de beslissing om te doneren. Verder gaven donoren die gedoneerd hadden aan iemand die ze kenden (relationele donoren) aan dat het lichamelijk en emotioneel functioneren van de ontvanger van hun nier sterk verbeterd was na de niertransplantatie, en dat hun eigen leven minder werd beïnvloed door de nieraandoening van de ontvanger dan voorafgaand aan de donatie. De relatie tussen de donor en ontvanger werd positief beoordeeld op alle meetmomenten. Uit deze studie kunnen we concluderen dat zowel algemene als ook donatie-specifieke meetinstrumenten waardevolle informatie bieden omtrent het functioneren van donoren. Beide geven aan dat de kwaliteit van leven van donoren in het algemeen niet tot nauwelijks negatief wordt beïnvloed door de donatie, hoewel een minderheid van donoren verhoogde niveaus van vermoeidheid, zorgen en gevoelens van spijt ten aanzien van de donatie rapporteert.

Tijdens de psychosociale screening voor de donatie wordt, naast het algemene emotionele functioneren, doorgaans ook de besluitvorming rondom de wens om te willen doneren besproken, waaronder de motivatie om te willen doneren, de verwachtingen van de donatie en mogelijke zorgen over de donatie die een rol spelen. Er is op dit moment echter geen betrouwbaar instrument dat alle drie deze thema's in kaart brengt, waardoor het niet mogelijk is om dit systematisch uit te vragen en om de voorspellende waarde hiervan te onderzoeken voor de kwaliteit van leven van donoren. Daarom werd een nieuwe vragenlijst ontwikkeld die deze thema's meet en werd de betrouwbaarheid van dit nieuwe meetinstrument onderzocht in een grote groep van 719 potentiële donoren uit zeven transplantatiecentra in Nederland. Dit onderzoek is beschreven in **Hoofdstuk 4.** De nieuw ontwikkelde vragenlijst, getiteld 'Donation Cognition Instrument' (in het Nederlands het 'Donatie Cognitie Instrument'), bestaat uit 31 items en is onder te verdelen in vijf categorieën: motivatie en verwachtingen omtrent een verbetering van het eigen welbevinden van de donor; 2) motivatie en verwachtingen rondom een verbetering van het welbevinden van de ontvanger; 3) idealistische motieven om

te doneren; 4) verwachtingen van dankbaarheid; en 5) zorgen rondom de donatie. Potentiële donoren gaven aan dat hun motivatie en verwachtingen van de donatie met name gericht waren op het verbeteren van het welbevinden van de ontvanger en minder op het verbeteren van hun eigen welbevinden. Er was een grote samenhang tussen de verschillende items uit de subschalen van de vragenlijst. Tevens werd een kleine tot middelmatige samenhang gevonden tussen de verschillende motivaties en verwachtingen rondom de donatie en algemene kwaliteit van leven. Het 'Donation Cognition Instrument' bleek een betrouwbaar instrument om de besluitvorming rondom de donatie in kaart te brengen en kan daarom een toegevoegde waarde hebben op de huidige psychosociale screening voor donoren.

Omdat een kleine groep donoren aangeeft problemen te ervaren voorafgaand of na de nierdonatie is het belangrijk om risicofactoren voor de ontwikkeling van problemen in kaart te brengen. Omdat er nog weinig onderzoek is gedaan naar de mate waarin demografische, medische en psychosociale kenmerken van donoren en het functioneren van de ontvangers voorspellend zijn voor langere termijn problemen bij donoren, is de psychosociale screening van donoren momenteel voornamelijk gebaseerd op de klinische indruk van zorgprofessionals. In hoeverre deze klinische indruk een goede inschatting geeft van het (toekomstige) functioneren van de donor is echter onbekend. Daarom werd onderzocht hoezeer de inschatting die zorgprofessionals maken ten aanzien van het risico van de donor op een minder goed functioneren na de donatie voorspellend was voor het daadwerkelijk functioneren van de donor. Ook werd onderzocht of vragenlijsten die door donoren zijn ingevuld zouden kunnen zorgen voor een optimalisering van de psychosociale screening. De resultaten zoals beschreven in **Hoofdstuk 5** laten zien dat de risico-inschattingen van zorgprofessionals voorspellend waren voor de daadwerkelijke kwaliteit van leven van donoren na de donatie. Dit bevestigt het belang en de juistheid van de klinische indruk als onderdeel van de donor screening. De toevoeging van donor zelfrapportage-vragenlijsten aan deze risico-inschattingen van zorgprofessionals zorgde voor een belangrijke verbetering van de voorspelling van langere-termijn problemen van donoren. Hierbij waren lichamelijke en emotionele klachten voorafgaand aan de donatie de belangrijkste voorspellers, wat de bevindingen uit de beperkte eerdere studies, zoals beschreven in Hoofdstuk 2, bevestigt. Daarnaast bleken verschillende specifieke cognitief-gedragsmatige factoren een (beperktere) rol te spelen in het voorspellen van kwaliteit van leven na donatie. Uit de resultaten kunnen we concluderen dat het opnemen van donor zelfrapportage-vragenlijsten de psychosociale screening van donoren kan verbeteren. Gebaseerd op de resultaten van dit onderzoek zou een stapsgewijze screening kunnen worden voorgesteld voor donoren, waarbij alle donoren een korte vragenlijst over lichamelijk en psychosociaal functioneren invullen tijdens de screening voor donatie of rondom de nacontrole na de

donatie. Als hieruit blijkt dat een donor een verhoogd risico heeft op problemen, dan zou een aanvullende screening kunnen worden uitgevoerd om te onderzoeken op welk gebied de donor problemen ervaart en welke psychosociale aspecten hierbij mogelijke aanknopingspunten bieden voor aanvullende ondersteuning.

Indien uit een screening zoals hierboven beschreven blijkt dat donoren een verhoogd risico op problemen hebben, dan zouden psychosociale interventies aansluitend op deze risicofactoren aanvullende ondersteuning kunnen bieden. Op basis hiervan is in **Hoofdstuk 6** de ontwikkeling en evaluatie beschreven van een psychosociale behandeling via internet voor donoren met een verhoogd risico op langere-termijn problemen na de donatie. Om relevante thema's voor de behandeling te vinden is gebruik gemaakt van de (relatief beperkte) kennis uit voorgaand onderzoek én zijn focusgroepen georganiseerd met donoren en zorgprofessionals om relevante thema's voor de behandeling in kaart te brengen. Een bestaande generieke behandeling voor patiënten met chronische somatische aandoeningen, waarin ook voor donoren relevante thema's zoals omgaan met lichamelijke beperkingen, vermoeidheid en angst centraal staan, werd met behulp van deze thema's (bijvoorbeeld besluitvorming rondom donatie, terugkeren in het dagelijks leven na de donatie, schuldgevoelens en sociaal-relationele problemen) aangepast zodat deze optimaal passend was voor de meest voorkomende mogelijke problematiek van (potentiële) donoren. In een kleine studie onder acht donoren werd een eerste evaluatie gedaan van de gebruiksvriendelijkheid en tevredenheid met de ontwikkelde behandeling. Donoren met een verhoogd risico op problemen werd eerst een face-to-face intakegesprek aangeboden waarin ze kennis maakten met hun therapeut en waarin doelen voor de behandeling werden geformuleerd. Hierna werd de gehele behandeling aangeboden via internet, waar donoren konden werken aan 1 of 2 behandelmodules, afhankelijk van hun behandeldoelen. Donoren konden een keuze maken uit de modules 'Lichamelijke beperkingen', 'Vermoeidheid', 'Negatieve stemming', 'Sociaal functioneren' en 'Algemene donatie-gerelateerde problemen'. Binnen deze modules kon de therapeut een keuze maken uit verschillende opdrachten en leesteksten, aansluitend op de doelen en uit de screening gebleken psychosociale sterke eigenschappen en aandachtspunten van de donor. De behandeling werd door de donoren positief geëvalueerd wat betreft de gebruiksvriendelijkheid en werkzaamheid. Deze resultaten zijn veelbelovend en laten zien dat een mogelijke implementatie van het zorgprotocol een toegevoegde waarde kan hebben in de psychosociale begeleiding van donoren.

De studies uit dit proefschrift richtten zich op het optimaliseren van de psychosociale zorg rondom de nierdonatie. De meeste donoren kunnen na de nierdonatie hun leven weer goed oppakken. Een minderheid ervaart echter wel enige problemen rondom de donatieprocedure, welke mogelijk met een goed onderbouwd zorgprotocol, bestaande uit een standaard screening en, indien geïndiceerd, een op de donor afgestemd begeleidingsprogramma ondersteund kan worden. In de toekomst zou onderzoek zich kunnen

richten op de (kosten)effectiviteit van het nieuwe eHealth zorgprotocol en zouden mogelijkheden moeten worden verkend om de nieuwe zorgproducten te implementeren in de klinische praktijk voor nierdonoren.

PUBLICATIONS

Wirken L, van Middendorp H, Hooghof CW, Sanders JSF, Dam RE, van der Pant KAMI, Wierdsma J, Wellink H, van Duijnhoven EM, Hoitsma AJ, Hilbrands, LB & Evers AWM. Consequences of living kidney donation: a prospective multicenter study. In revision.

Wirken L, van Middendorp H, Hooghof CW, Bremer TE, Hopman SPF, van der Pant KAMI, Hoitsma AJ, Hilbrands, LB & Evers AWM. Development and feasibility of a guided and tailored internet-based cognitive-behavioral intervention for kidney donors and kidney donor candidates. In revision.

Wirken L, van Middendorp H, Hooghof CW, Sanders JSF, Dam RE, van der Pant KAMI, Wierdsma J, Wellink H, Ulrichts PTR, Hoitsma AJ, Hilbrands, LB & Evers AWM. Combining transplant professional's psychosocial evaluation and donor self-report measures to optimize the prediction of HRQoL after kidney donation: a prospective multicenter study. Submmitted.

Wirken L, van Middendorp H, Hooghof CW, Sanders JSF, Dam RE, van der Pant KAMI, Berendsen ECM, Wellink H, Dackus HJA, Hoitsma AJ, Hilbrands, LB & Evers AWM. (2017). *Nephrology Dialysis Transplantation*, 32 (3): 573-580.

Wirken L, van Middendorp H, Hooghof CW, Rovers MM, Hoitsma AJ, Hilbrands, LB & Evers AWM. (2015). *The American Journal of Transplantation*, 15 (12): 3041-54.

Wirken L, van Middendorp H & Evers AWM. (2014). Psychologische aspecten rondom nierdonatie bij leven. *Cahier 'Je nier of mijn leven!'* Stichting Biowetenschappen en maatschappij.

Evers AWM, Verhoeven EW, van Middendorp H, Sweep FC, Kraaimaat FW, Donders AR, Eijsbouts AE, van Laarhoven AI, de Brouwer SJ, **Wirken L**, Radstake TR & van Riel PL. (2014). Does stress affect the joints? Daily stressors, stress vulnerability, immune and HPA axis activity, and short-term disease and symptom fluctuations in rheumatoid arthritis. *Annals of Rheumatic Diseases*, 73 (9):1683-1688.

van Koulil S, van Lankveld W, Kraaimaat FW, van Helmond T, Vedder A, van Hoorn H, Donders AR, **Wirken L**, Cats H, van Riel PL & Evers AWM. (2011). Tailored cognitive-behavioural therapy and exercise training improves the physical fitness of patients with fibromyalgia. *Annals of Rheumatic Diseases,* 70 (12):2131-2133.

PHD PORTFOLIO

Institute for Health Sciences
Radboudumc

Name PhD candidate: L. Wirken	PhD period: 01-06-2011 – 05-12-2017
Department: Medical Psychology	Promotors: Prof. A.W.M. Evers
Graduate School: Radboud Institute for Health Sciences	Prof. L.B. Hilbrands
	Prof. A.J. Hoitsma
	Co-promotor: Dr H. van Middendorp

	Year(s)	ECTS
TRAINING ACTIVITIES		
a) Courses & Workshops		
- RIHS Introduction Course	2011	1.75
- Workshop Endnote Radboudumc	2011	0.1
- Basiscursus Regelgeving en Organisatie voor Klinisch Onderzoekers (BROK)	2012, 2016	1.95
- Biometrics Course	2012-2013	4.0
- RIHS Course 'How to organise your data'	2012	0.1
- RIHS Workshop 'How to design your thesis'	2013	0.1
- RIHS Workshop 'How to convince the editor'	2013	0.1
- Academic Writing Course Radboudumc	2013-2014	3.25
- Workshop Social Media and Disruptive Technology Radboudumc	2015	0.1
- Teaching Workshop – 'Teaching and Enhancing Student Learning' Leiden University	2015	0.1
- Teaching Workshop – 'Getting a response from your audience' Leiden University	2015	0.1
- SOLO Workshop Want to write a social-scientific blog?	2016	0.2
- Workshop Festivalpitchen, Raboudumc	2017	0.1
b) Seminars & Lectures		
- Transplantatiebijeenkomst afdeling Nierziekten (oral)	2011	0.1
- Transplantatieteam Kindernefrologie (oral)	2012	0.1
- Refereeruur Department of Nephrology, Radboudumc (oral)	2013	0.1
- Themadag Nierdonoren, Nierpatienten Vereniging Nederland (invited speaker)	2015	0.5
- Nascholing Psychosociale Nefrologie, Radboudumc (invited speaker)	2015	0.2
- Food for Thought Meeting – Leiden University (laptop)	2016	0.1
- Leiden University – LUMC eHealth meeting (oral)	2016	0.5
- Nascholing Nefrologie Papendal (invited speaker)	2016	0.5
c) Symposia & Congresses		
- Working group Social Sciences kidney diseases	2011	0.5
- RIHS PhD retreat, Wageningen (poster)	2011	0.75
- Symposium Psychology & Medicine (visitor)	2011	0.2
- ARPH Conference, Lunteren (poster)	2011	1.0
- Kwaliteitsmiddag - Social media in de zorg (visitor)	2012	0.2
- Bootcongres Dutch Transplant Society, Maastricht (visitor)	2012	1.0
- RIHS Annual Science Day (visitor)	2012	0.2

- Symposium Nierdonatie bij leven UMCG (invited oral)	2012	0.5
- RIHS PhD retreat, Wageningen (oral)	2012	1.0
- NBMF Netwerkdag (visitor)	2012	0.5
- ISRII, Utrecht (laptop)	2012	0.2
- Conferentie Orgaandonatie; geschenk of offer, Radboudumc (visitor)	2012	0.75
- Symposium niertransplantatie; beter en meer! Radboudumc (visitor)	2012	0.2
- ARPH Conference, Enschede (poster)	2013	1.0
- Bootcongres Dutch Transplant Society, Duiven (laptop)	2013	1.0
- ELPAT Congress, Rotterdam (poster)	2013	1.75
- RIHS Science Day (visitor, PhD Council)	2013	0.2
- ARPH Conference, Groningen (oral)	2014	1.0
- Bootcongres Dutch Transplant Society, Leiden (oral)	2014	1.5
- Leiden Institute for Brain and Cognition, LIBC Dag (poster)	2014	0.5
- ICBM Congress, Groninigen (oral)	2014	1.5
- LIBC publiekssymposium (visitor)	2014	0.5
- Publieksavond Nier op Maat – Radboudumc (visitor)	2014	0.2
- Leiden Institute for Brain and Cognition, LIBC Dag (visitor)	2015	0.2
- NSRII Symposium, Leiden (laptop)	2015	0.2
- Bootcongres Dutch Transplant Society, Groningen (oral)	2016	1.0
- ELPAT Congress, Rome (2x oral)	2016	1.75
- Dutch Transplant Society, Young Professionals in Transplantation (oral)	2016	0.5
- ARPH Conference, Leiden (oral & poster)	2017	1.0
- Bootcongres Dutch Transplant Society, Zeist (visitor)	2017	1.0
d) Other		
- Werkgroep Sociaal Wetenschappelijk Onderzoek Nefrologie	2011-present	1.0
- Junior Researchers Seminar Radboudumc Medical Psychology	2011-2013	1.5
- Junior Researchers Seminar Radboudumc 'eHealth Support Committee (ESC)'	2011-2013	1.0
- RIHS PhD Council member	2013	1.0
- Journal reviewer 'American Journal of Transplantation'	2016	0.1

TEACHING ACTIVITIES

e) Lecturing

- Leiden University: Bachelor Psychology course 'Perspective on Career Planning' (POCP) – seminar teacher	2017	5.0
- Leiden University: Bachelor Psychology course 'Health and Medical Psychology'	2017	2.0

f) Supervision of internships / other

- Thesis supervisor Master Medical Sciences Radboud University. Thesis:	2013	1.0
- Thesis supervisor Master Health Psychology, Leiden University. Thesis: Living Kidney Donation: A Prospective Study on the Predictive Role of Pre-donation Cognitions on Longer-term Health-Related Quality of Life of Living Kidney Donors	2014-2015	1.0
- Thesis supervisor Master Health Psychology, Leiden University. Thesis: The donor – recipient relationship in living donor kidney transplantation: a prediction model of health-related quality of life, anxiety and depression	2016-2017	1.0
- Thesis supervisor Master Health Psychology, Leiden University. Thesis: Predictors of longer-term fatigue after living kidney donation	2017	1.0
TOTAL		**51.45**

DANKWOORD (ACKNOWLEDGEMENTS)

Heel graag wil ik iedereen bedanken die betrokken is geweest bij de totstandkoming van mijn proefschrift.

Allereerst wil ik alle (potentiële) donoren bedanken voor hun inzet voor het onderzoek. Het was ontzettend mooi om jullie belangstelling in wetenschappelijk onderzoek en jullie actieve bijdrage aan het project te zien. Alle mensen die belangeloos vragenlijsten hebben ingevuld, deel hebben genomen aan focusgroepbijeenkomsten en/of de eHealth interventie hebben gevolgd en geëvalueerd, ontzettend bedankt!

Een speciaal woord van dank gaat uit naar mijn promotieteam: prof. dr. Andrea Evers, prof. dr. Luuk Hilbrands, prof. dr. Andries Hoitsma en dr. Henriët van Middendorp.

Beste Andrea, in 2008 startte ik met het schrijven van mijn master thesis binnen jouw onderzoeksgroep, met het idee om na afronding van mijn thesis in de klinische praktijk te gaan werken als psycholoog. Het is wat anders gelopen! Na participatie in verschillende onderzoeksprojecten (van het uitvoeren van data-analyses tot werken als eCoach therapeut) kwam dit promotieonderzoek op ons pad. Bedankt voor het vertrouwen en de vele kansen die je me hebt geboden om mezelf steeds verder te ontwikkelen.

Beste Luuk, veel dank voor je betrokkenheid bij dit onderzoek vanuit het nefrologisch perspectief. Ik heb ontzettend veel geleerd van je kritische en klinische blik op de onderzoeksresultaten en de interpretatie hiervan. Beste Andries, bedankt dat je het hebt mogelijk gemaakt om deze studie te initiëren binnen de afdeling Nierziekten van het Radboudumc. Tijdens het onderzoeksproject ging je met emeritaat, maar je bleef gelukkig actief betrokken in de projectgroep. Veel dank voor je commentaar op alle stukken en je actieve rol in de dataverzameling van de medische gegevens van de ontvangers vanuit de NOTR.

Beste Henriët, in ons wekelijks overleg was het superfijn om, naast de inhoudelijke aspecten van mijn onderzoek, ook meer persoonlijke zaken te bespreken. Jouw humor en positieve houding was erg inspirerend en heeft me ontzettend geholpen bij tegenslagen! Jouw gedetailleerde feedback heeft de kwaliteit van mijn publicaties sterk bevorderd, heel veel dank hiervoor.

Prof. dr. Lagro-Janssen, beste Toine, via het mentorschap van NCEBP kwamen we met elkaar in contact. Dank voor je persoonlijke begeleiding, het was ontzettend prettig om tijdens mijn promotie-traject onderzoeks-strubbelingen, persoonlijke worstelingen, maar zeker ook persoonlijke groei te kunnen bespreken.

Een speciaal woord van dank voor Yvonne Hooghof, want zonder jouw initiatief om tijdens jouw functioneringsgesprek als verpleegkundig coördinator nierdonatie bij leven binnen het Radboudumc de psychosociale zorg voor nierdonoren onder de aandacht te brengen had dit onderzoeksproject waarschijnlijk helemaal niet plaatsgevonden. Dank je wel voor het meedenken over de vormgeving van het project, en voor al jouw inzet in

de werving van donoren en de dataverzameling. Je bent een fijne collega, en ik ben er trots op dat je op de dag van de promotie aan mijn zijde staat als paranimf.

Desiree Pilzecker, Ine Dooper, Heinrich Kloke, Sabine Hopman, Gerben van den Bosch en Simon van Duin; samen met Yvonne vormen jullie het sterke donorteam van het Radboudumc. Dank voor jullie enthousiaste inbreng in het onderzoek, het benaderen van donoren, het invullen van de risicoprofielen en het meedenken over de keuze van vragenlijsten en de inhoud van de eHealth interventie voor donoren. Ik heb me erg welkom gevoeld in jullie hechte team en heb met veel plezier de transplantatiecongressen met jullie bijgewoond!

Daarbij aansluitend wil ik graag alle coördinatoren nierdonatie bij leven uit de overige participerende transplantatiecentra bedanken: Tessa de Jong-Pulskens, Janneke Vervelde (AMC), Regien Meijer, Ellen Jansen, Annemarie Roelofs, Dominique Rodenhuis, Juliette Rabbeljee (UMCG), Ruth Dam (LUMC), Philip Ulrichts, John Dackus (azM), Judith Wierdsma, Elsbeth Berendsen (UMC Utrecht), Hiske Wellink, Marjon van Vliet en Carla Schrauwers (VUmc). Veel dank voor jullie inzet bij de inclusie van donoren en het aanleveren van gegevens! Ik vind het bewonderenswaardig hoe jullie deze studie hebben opgepakt naast alle logistiek die komt kijken bij de zorg rondom de nierdonatie. Tevens veel dank aan de betrokken nefrologen voor het faciliteren van dit onderzoek op de afdelingen Nefrologie in de verschillende centra: Jan-Stephan Sanders (UMCG), Karlijn van der Pant (AMC), Elly van Duijnhoven (azM), Franka van Reekum (UMC Utrecht), Azam Nurmohamed (VUmc), en de medisch maatschappelijk werkers die betrokken waren bij het project: Tanneke Winkel (UMC Utrecht), Ben Gijsbers, Wilma van Zanten (LUMC), Manon Meijer, Gert-Jan Hersbach (VUmc) en Michel Knaapen (azM). Veel dank voor het invullen van alle risico-inschattingsvragenlijsten!

Mijn promotieonderzoek startte op de afdeling Medische Psychologie van het Radboudumc. Ik heb hier een ontzettend fijne tijd gehad. Een speciaal woord van dank voor mijn kamergenootjes: Sylvia, Maaike, Judith, Sanne, Annemiek, Saskia, Antoinette en Sabine; het was erg fijn om alle leuke en minder leuke momenten die samengaan met het doen van onderzoek met jullie te delen. Ook de medewerkers van het secretariaat (Helma, Nancy, Jacintha, Brenda en Joost) veel dank voor alle praktische ondersteuning en de gezellige momenten. Tamara Bremer, veel dank voor jouw inzet en de fijne samenwerking bij de eHealth studie; wat was ik blij met jou als therapeut op dit project!

In 2014 maakte onze onderzoeksgroep de overstap naar de Universiteit Leiden. Een nieuw begin binnen een heel andere werksetting dan in het ziekenhuis. Ik heb me ontzettend welkom gevoeld op de afdeling Gezondheids-, Medische en Neuropsychologie. Alle collega's met wie ik in onderwijs of onderzoek heb samengewerkt; veel dank hiervoor!

Natuurlijk vooral de collega's op de AIO gang met in het speciaal: Judith, Kaya, Sylvia, Danielle, Roos en de nier-onderzoekers Yvette, Katja en Judith!

Ook buiten mijn werk heb ik veel belangstelling voor mijn onderzoek en steun ervaren van de mensen om me heen. Mijn 'Nijmegense' vriendinnen Hester, Lotte B, Lotte M en Sarah, we hebben al vanaf de introductie van de studie Psychologie een hechte band die voor mij heel waardevol is. Ook al zien we elkaar niet dagelijks meer, ik kijk er altijd naar uit om jullie weer te zien! Hester, naast vriendin ben je ook een collega waar ik veel bewondering voor heb. Ik ben er trots op dat je mijn paranimf bent!

Lieve Jelle en Stefanie, samen hebben we al veel mooie, maar helaas ook moeilijke momenten gedeeld. Jullie positieve manier van in het leven staan vind ik heel bijzonder! Onze vriendschap is mij ontzettend veel waard, dank jullie wel daarvoor!

Dan mijn muzikale vrienden van de VTR, Sandra, Roy, Karin, Mark, Lian, Tom, Rob, Bert, Rolf, Niels, Eelke, Manon, Paula, Dirk-Jan, Rob, Frank en Tim, het is altijd gezellig om met jullie op te treden en te repeteren. Dank jullie wel voor alle leuke (muzikale en niet muzikale) momenten!

Mijn schoonfamilie, Cees en Addy, Rozanne en Tim, dank jullie wel voor jullie interesse in mijn onderzoek, en dat we altijd welkom zijn! De gezellige vrijdagavond-etentjes zijn een fijn begin van het weekend na een drukke werkweek.

Lieve papa en mama, bedankt dat jullie altijd achter me staan! Jullie hebben ervoor gezorgd dat ik hier nu sta, door te geloven in mijn kwaliteiten en deze te stimuleren. Jullie hebben me geleerd om door te zetten als ik echt iets wilde bereiken en dat waardeer ik ontzettend. Bedankt voor alles wat jullie voor ons doen! Sanne en Bram, Joost en Tanya, dank jullie wel voor de fijne band die we met elkaar hebben.

Lieve Liv, Stef en Siebe, ik ben er trots op dat ik jullie tante ben!

Lieve Floris en Lucas, thuiskomen bij jullie na een drukke dag is het fijnste wat er is. Lucas, mama is supertrots op jou, je vrolijkheid, nieuwsgierigheid en eigenwijsheid brengen jou vast heel ver! Floris, dank je wel voor al je steun, relativeringsvermogen, humor en het bewaken van de balans tussen werk en privé. Een promotietraject is op zichzelf al pittig, maar tegelijkertijd een huis bouwen, daar moet je samen sterk voor staan. Op naar het volgende hoofdstuk in ons leven!

Lieke

CURRICULUM VITAE

Lieke Wirken werd op 13 januari 1985 geboren te Dongen, waar zij ook opgroeide. Na het behalen van haar gymnasiumdiploma aan het Sint Oelbertgymnasium te Oosterhout in 2004 verhuisde ze naar Nijmegen om Psychologie te studeren aan de Radboud Universiteit. Ze koos voor de afstudeerrichting Klinische Psychologie die in 2009 werd afgerond, waarbij zij haar Masterscriptie schreef over Stress bij patiënten met Reumatoïde Artritis op de afdeling Medische Psychologie van het Radboudumc. Na haar afstuderen (2009-2010) bleef zij als projectmedewerker werkzaam in het Radboudumc op de afdelingen Medische Psychologie, Eerstelijnsgeneeskunde en Revalidatie en was zij betrokken bij verschillende onderzoeksprojecten bij patiënten met chronisch somatische aandoeningen, ouderen en mensen met een verstandelijke beperking. In 2010 en 2011 was zij werkzaam als psycholoog op de afdeling Reumatologie van de Sint Maartenskliniek te Nijmegen, waar zij individuele en groepsbehandelingen gaf aan mensen met reumatische aandoeningen. Daarnaast is zij op de afdeling Medische Psychologie van het Radboudumc als therapeut betrokken geweest bij onderzoeksprojecten naar cognitieve gedragstherapie via internet bij patiënten met reumatische aandoeningen en huidaandoeningen.

In 2011 werd zij aangesteld als promovendus op de afdeling Medische Psychologie van het Radboudumc, waar ze een door de Nierstichting gefinancierd onderzoek heeft gedaan naar de ontwikkeling van een psychosociaal screeningsinstrument en psychosociale interventie via het internet voor nierdonoren in zeven transplantatiecentra in Nederland, zoals in dit proefschrift beschreven. Dit onderzoek maakte deel uit van de onderzoeksschool Radboud Institute for Health Sciences (RIHS). Tijdens haar promotieonderzoek heeft zij diverse presentaties verzorgd op nationale en internationale congressen binnen de Transplantatie en Psychologie. Tevens was zij in 2013 actief als algemeen lid van de PhD Council van RIHS.

In 2014 volgde zij haar eerste promotor en co-promotor naar de Sectie Gezondheids-, Medische en Neuropsychologie aan de Universiteit Leiden, waar zij haar promotieonderzoek voortzette en tevens als docent werd aangesteld.

Momenteel is Lieke Wirken werkzaam binnen de sectie Gezondheids-, Medische en Neuropsychologie aan de Universiteit Leiden, waar ze als vervolg op haar promotieproject de implementatie van een eHealth psychosociaal zorgprotocol bij nierdonoren in verschillende transplantatiecentra in Nederland onderzoekt, gefinancierd door de Nierstichting. Tevens is zij aangesteld als docent binnen de Bacheloropleiding Psychologie en Masteropleiding Gezondheids-, Medische en Neuropsychologie aan de Universiteit Leiden. Ze is getrouwd met Floris Beerens en zij hebben een zoon Lucas (2015).

Institute for Health Sciences

Radboudumc